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THE TREATMENT OF INFECTIONS AND INFECTIOUS DISEASES WITH MERCUROCHROME-220 SOLUBLE

AN ANALYSIS OF TWO HUNDRED AND TEN CASES THAT FURNISH MANY DEFINITE EXAMPLES OF A THERAPIA STERILISANS MAGNA *

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EARLY ATTEMPTS AT BRADY INSTITUTE TO PRODUCE AN INTRAVENOUS GERMICIDE

During the last eight years the research work in the laboratory of the Brady Urological Institute has been largely concerned with the development of germicides and antiseptics. Starting with an effort to make a compound of phenolsulphonephthalein which, when injected intravenously, would act as a genito-urinary germicide, investigation was broadened to an exhaustive study of many dyestuffs and compounds from them. In this work, E. C. White, E. G. Davis and E. O. Swartz cooperated with us in chemical and bacteriologic experimental and clinical studies, many of which have been published. Impressed with the possibilities of using dyes as a basis for the development of therapeutic compounds, we have concentrated our efforts on the production of new drugs possessing the penetrating qualities of dyes which are, at the same time, germicidal and relatively nontoxic and nonirritating, so that they can be introduced intravenously with safety in germicidal or bacteriostatic strength. Among the more than 260 compounds that have been prepared by E. C. White and studied by us and our confrères, mercurochrome-220 soluble has proved to be a germicide of great value.

MERCUROCHROME-220 SOLUBLE

The literature concerning this is already very extensive. In our first paper,[1] we stated:

> Since the tissues are generally more sensitive to acidity than to alkalinity, this reasoning led to the choice of an acid dye as the basis of the synthetic germicide.

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* From the James Buchanan Brady Urological Institute, Johns Hopkins Hospital.

1. Young, H. H.; White, E. C., and Swartz, E. O.: A New Germicide for Use in the Genito-Urinary Tract: "Mercurochrome-220," J. A. M. A. **73**: 1483-1491 (Nov. 15) 1919.

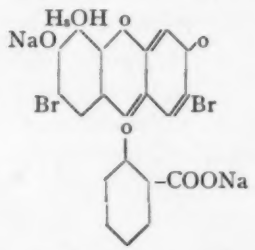
The extensive use of eosin as a cytoplasmic stain at once suggested its use as a suitable dye of this class. However, it does not lend itself to chemical modification because those positions in its molecule susceptible to substitution by other chemical groups are already occupied by bromin. On the other hand, it was found that the closely related substance dibromfluorescein could undergo substitution by the germicidal group we chose and still retain practically the same tinctorial properties that eosin itself possesses.

Mercury was chosen as the active germicidal principle to be substituted in the dye molecule.

The irritating effect of solutions of mercuric chlorid is due to the mercury ion. If, however, the metal is substituted in an organic compound, such as an acid dye, the mercury no longer yields ions but exists as a firmly bound part of the dye molecule itself. In this form of combination, the properties of the metal as manifested by mercury salts are more or less completely masked. The new substance gives a negative reaction with the usual reagents for mercury, such as alkalis, iodids and alkali sulphids.

CHEMISTRY

To the substance obtained by substituting one atom of mercury in the molecule of dibromfluorescein we have given the name mercurochrome-220. Chemically it is dibromoxymercuryfluorescein or its sodium salt. The latter contains about 26 per cent. of mercury, and is represented by the formula:



The free acid is a red powder insoluble in water but readily soluble in sodium hydroxid solution, with the formation of a deep cherry red color, showing fluorescence on dilution. The dry salt forms iridescent green scales, slightly hydroscopic and readily soluble in water. The solution is stable and is not affected by moderate heat or exposure to the air. Strongly acid urine (p_H 5.0) gives a slight precipitate of the free dye; but if the acidity is p_H 6.4 or less, no precipitation occurs. There is entire freedom from precipitation when a 1 per cent. solution of the drug is mixed with an equal volume medium rich in protein, such as hydrocele fluid.

PENETRATION AND STAINING QUALITIES

After making frozen and paraffin sections of the urethra, bladder, kidneys and ureters of rabbits following the local injection of 1 per cent. mercurochrome-220, Young, White and Swartz [1] report the following findings:

Examination of the frozen sections as well as of the paraffin sections shows that the epithelial cells of the urethra are stained a deep red. This staining is most intense in the superficial layer and becomes less intense toward the submucosa; but the submucosa was stained in places, though not so uniformly

as the epithelial layers. In some places the stain penetrated the submucosa into the muscularis. This mercury-bearing dye stains the epithelium of the anterior and posterior urethra uniformly, and to a less extent penetrates to the submucous layers. Sections of the bladder and the ureter show the same uniform penetration and staining of the cytoplasm of the epithelial cells, and the submucosa is less deeply stained. Sections of the kidney pelvis showed penetration and staining of the epithelium. The dye had also been taken up by the cells of the collecting tubules, and they were stained for a short distance up the tubules from the papillae. In the urethra, the epithelium of the glands opening into the urethra was stained for some distance from the mouths of the ducts.

TOXICITY, IRRITATION AND EFFECT ON KIDNEY

In the original paper by Young, White and Swartz, the following report on toxicity was made:

> We noticed a variation in the amount of the drug that rabbits and dogs could tolerate. Ten milligrams per kilogram invariably killed rabbits in twenty-four hours, and no gross lesions were found at necropsy. Rabbits receiving 5 mg. per kilogram showed a decrease in phenolsulphonephthalein and an albuminuria that lasted about a week. Dogs tolerated 10 mg. per kilogram very well with no evidence of discomfort or illness. In each instance, there was produced an albuminuria without casts and a temporary reduction in phenolsulphonephthalein output but no rise in blood urea. The albuminuria persisted about five days. At no time were casts found. The phenolsulphonephthalein output returned to normal with the disappearance of the albuminuria. No evidence of kidney damage was found at necropsy on an animal killed at the end of the experiments.

Subsequent experiments have shown that it could be injected into the same vein repeatedly without causing irritation, and that the drug was of about the same toxicity to the human being as to rabbits and slightly more toxic than for dogs. Human beings have in scores of instances been injected with doses of 5 mg. per kilogram of body weight without apparent injury. We have, in several instances, used doses of 6, 7 and even 8 mg. per kilogram. In the larger doses, reactions are usually characterized by nausea, vomiting and frequent stools. In fact, such reactions have occurred even when much smaller doses have been used. On the other hand, some patients have received large doses, even as much as 7.5 mg. per kilogram without many gastro-intestinal reactions. The subject will be discussed at greater length further on.

The effect of the drug on the kidneys at once occupied our attention and, as mentioned above, it was shown that, even when lethal doses were given to animals, the kidneys showed little or no change macroscopically and microscopically. Careful studies of the urine of patients who received large doses sometimes showed slight albuminuria and occasionally a few casts, but in all cases studied by us these have disappeared in a few days. Even when 7.5 mg. per kilogram was used, it was shown that, in the presence of albumin and casts as a result of urinary infection,

the content of albumin was not increased, but in some instances pus cells and the urinary infection disappeared after an intravenous injection of mercurochrome-220.

Our studies [2] of the effect of mercurochrome-220 on the kidneys of animals is shown in the accompanying illustrations. Single injections of 1, 2.5, 5, 7.5 and 10 mg. per kilogram were given, the animals being killed two days after treatment. In addition, two series of treatments were given, consisting of twelve injections of 1, 2.5 and 5 mg. per

Fig. 1.—Kidney section of Rabbit 1 made two days after one intravenous injection of 1 mg. per kilogram of mercurochrome-220 soluble. For Figures 1 to 7 we are indebted to the *Bulletin of Johns Hopkins Hospital.*

kilogram, two a week, the animals in one series being killed two days after the last injection, those of the other series being held two months and then killed. The conclusions were:

Intravenous injection of mercurochrome-220 causes a mild reaction in the kidney which is directly proportional to the dose given. There is no actual destruction of tubular epithelium from doses as high as 7.5 mg. per kilogram, but with 10 mg. per kilogram there is definite renal damage, so that it would be unwise to use so large a dose clinically. Repeated injections do not cause any added damage, and may be given, as in these animals, as often as twice a week with safety, provided a dose of 5 mg. per kilogram be not exceeded. The slight damage is not irreparable and, at the end of two months, the kidneys show no evidence of any previous lesion.

2. Hill, J. H., and Bidgood, C. Y.: Bull. Johns Hopkins Hospital **35**:409 (Dec.) 1924.

Figures 1, 2 and 3 show sections from the kidneys of rabbits which received repeated intravenous injections and which were killed two days after the last dose.

Studies of other organs of animals have also revealed no damage of any moment. Clinical experience, in a moderate number of cases, has shown stomatitis, varying in character from slight to violent, accompanied by marked changes in the mucous membrane, gums, looseness of teeth and salivation. In one of our cases, this was very pronounced and gave the patient great discomfort, but even in this case the condition cleared up completely.

Fig. 2.—Kidney section of Rabbit 2 made two days after one intravenous injection of 2.5 mg. per kilogram of mercurochrome-220 soluble.

No irritation followed application of mercurochrome-220 in a 1 per cent. solution in the conjunctival sac of rabbits. Five per cent. solution in the urethra and in the bladder caused only temporary burning, and 1 per cent. solution in the kidney pelvis was followed by no reaction in many cases.

In clinical usage, a 1 per cent. solution has been injected into the bladder and urethra four times a day for several consecutive days without producing more than slight irritation.

The 1 per cent. drug has been used in the ear, nose, throat and mouth with only slight transitory irritation. It has been used with impunity in a 1 per cent. solution in open wounds and in granulating cavities in which free drainage was present. In a fresh wound, stomatitis, in rare

instances, has come on from the absorption of the wound, but as a result of extensive animal experiments and usage in clinical cases, we may say that mercurochrome-220 may be employed in relatively strong solutions and at frequent intervals with remarkably low irritation and practically no danger.

Fig. 3.—Kidney section of Rabbit 3 made two days after one intravenous injection of 5 mg. per kilogram of mercurochrome-220 soluble.

GERMICIDAL STUDIES IN VITRO

Our original studies[1] showed the germicidal action of mercurochrome-220 in urine and in serum (hydrocele fluid). For the details of the method, the reader is referred to our original article. The results of these tests are expressed in Table 1.

TABLE 1.—*Germicidal Strength of Mercurochrome-220 in Urine*

Medium	Organism	Time Exposed to Drug	Highest Dilution Killing Uniformly
Urine ($p_H = 6.4$)	B. coli	1 minute	1:800
	B. aureus	1 minute	1:1,000
	B. coli	5 minutes	1:1,000
	S. aureus	5 minutes	1:5,000
	B. coli	15 minutes	1:5,000
	B. aureus	15 minutes	1:10,000
	B. coli	1 hour	1:5,000
	S. aureus	1 hour	1:10,000
	B. coli	24 hours	1:20,000
	S. aureus	24 hours	1:20,000
Hydrocele fluid	B. coli	1 hour	1:1,000
	S. aureus	1 hour	1:1,000
	B. coli	24 hours	1:4,000
	S. aureus	24 hours	1:4,000

Our conclusions were as follows:

The outstanding fact observed on comparing the germicidal values of mercurochrome-200, acriflavine, protargol and argyrol is the rapidity of action of mercurochrome-220 in fairly high dilutions. In one minute it kills *B. coli* or *Staphylococcus aureus* in a dilution of about 1:1,000, a result obtained with none of the other drugs, even in one hour. In fifteen minutes its effect is nearly as great as in twenty-four hours, killing *B. coli* in this short time at 1:5,000, and *Staphylococcus aureus* at 1:10,000. A few tests were made to learn the minimal time in which a 1:100 solution would sterilize. *Staphylococcus aureus* was killed almost instantaneously (no longer than ten seconds). The same test on *B. coli* revealed that a few organisms remained after ten seconds' exposure to the drug. Since a 1:800 solution kills this organism in one minute, the time necessary for a 1:100 solution to kill is possibly no more than thirty seconds.

Whereas both argyrol and protargol at 1:1,000 fail to kill either *B. coli* or *Staphylococcus aureus* in one hour, the same concentration of the mercury dye kills both organisms in about one minute.

Tests of the action of mercurochrome-220 on the gonococcus in our laboratories[3] showed that a five minute exposure killed the organisms in a dilution of 1:4,000, but failed in a dilution of 1:6,000. A twenty minute exposure killed in a dilution of 1:16,000, but failed in 1:32,000. Twenty minute tests on *B. coli* by the same technic showed complete killing in a dilution of 1:400, but failure in 1:800. Twenty minute tests on *Staphylococcus aureus* by the same method showed only 2 colonies after exposure to 1:50 dilution. The reasons for the difference between these figures and those of the original paper[1] are discussed by Davis and Swartz,[4] the number of organisms used and the presence of protein being important considerations.

In a later paper,[5] we gave additional information about the germicidal action of mercurochrome-220 in 50 per cent. dog serum and 0.875 per cent. sodium chlorid solution. Three strains were used of some of the organisms tested, in order to establish probable ranges of specific variation of resistance. The three strain average killing power of mercurochrome-220 against *B. coli* is 1:100 in one minute in 50 per cent. serum; 1:150 in one minute in salt solution; 1:500 in one hour in serum, and 1:100,000 in one hour in salt solution. Against three strains of *Staphylococcus aureus,* the average killing dilution in one minute was 1:90 in salt solution and serum; 1:200 in one hour in serum, and 1:100,000 in one hour in salt solution. Against *Pseudomonas pyocyanea* and *B. pneumoniae,* the action in one minute is much less, but in one hour is 1:200 against *Pseudomonas pyocyanea* in serum, 1:100,000 in salt solution; against *B. pneumoniae,* 1:500 in one hour in serum, 1:70,000 in salt solution.

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3. Swartz, E. O., and Davis, D. M.: Action of Mercurochrome-220 on the Gonococcus, J. A. M. A. **76**:844-846 (March 26) 1921.

4. Davis, D. M., and Swartz, E. O.: J. Infect. Dis. **27**:951-601 (Dec.) 1920.

5. Young, H. H.; White, E. C.; Hill, J. H., and Davis, D. M.: Surg., Gynec. & Obst. **36**:508-521 (April) 1923.

ANTISEPTIC ACTION IN BLOOD AND URINE

For the effect of intravenous injection of mercurochrome-220 on the bacteriostatic action of blood, studies were made of normal rabbits, which were injected in one ear with freshly prepared solution of the drug.[6] Single doses of 1, 2.5, 5 and 7.5 mg. per kilogram were given. One minute before injection and fifteen, thirty, forty-five and sixty minutes after injection, measured specimens of blood were removed from the opposite, uninjected ear, brought to a total volue of 2 c.c. with sterile sodium citrate solution and inoculated with a standard loopful of a twenty-four hour beef infusion (p_H 7.6) broth culture of *B. coli*. Thirty seconds after inoculation, 0.1 c.c. of the organism-blood mixture was removed, dilutions in 0.875 per cent. sodium chlorid were made and plates poured to determine the number of organisms per cubic centimeter present at the time of inoculation. In these experiments, it has been shown that, following the intravenous injection of mercurochrome-220, the bacteriostatic action of blood against *B. coli* is increased. This increase appears to be greatest from fifteen to forty-five minutes after the injection, after which it rapidly disappears.

Clinical experiments, which will be detailed at length further on, have shown that, in some instances, a remarkable sterilizing effect on the blood may be obtained by the intravenous injection of mercurochrome-220. In one case in which the patient received an intravenous injection of 7.5 mg. per kilogram of 1 per cent. mercurochrome-220, *Streptococcus hemolyticus* was eliminated from the blood within twelve hours, the cultures after that time remaining sterile. In other cases in which 5 and even 2 and 3 mg. per kilogram were used, the blood, previously infected with various organisms (streptococci, staphylococci, diplococci and bacilli), has been found sterile. These clinical reports will form the basis of the major part of our paper and will be detailed at length.

Bacteriostatic and bactericidal action in urine after intravenous injection of mercurochrome-220 has been shown experimentally in rabbits, with varying results.[7] In one case in which only 1 mg. per kilogram was given, the urine taken two hours after intravenous injection of mercurochrome-220 was bactericidal. The second case of bactericidal action was after an injection of 5 mg. per kilogram, the specimen one hour after administration killing the inoculum (4,700,000 organisms per

6. Hill, J. H., and Colston, J. A. C.: Bull. Johns Hopkins Hosp. **34**:372 (Nov.) 1923.

7. Hill, J. H., and Colston, J. A. C.: Bull. Johns Hopkins Hosp. **34**:220 (July) 1923.

cubic centimeter) in a twenty-four hour exposure. The drug was injected into the ear vein in 1 per cent. solution. Urine was obtained by catheterization aseptically five minutes before injection and at intervals of one, two, five and twenty-four hours after injection. Of each specimen, 0.1 c.c. was plated to serve as a preinoculation sterility control. Of each specimen, 2 c.c. was put into a sterile tube and inoculated with one standard loopful of a twenty-four-hour culture of *B. coli* in p_H 7.6 dextrose broth. Thirty seconds, one, two and twenty-four hours after inoculation, 0.1 c.c. of the organism-urine mixture was

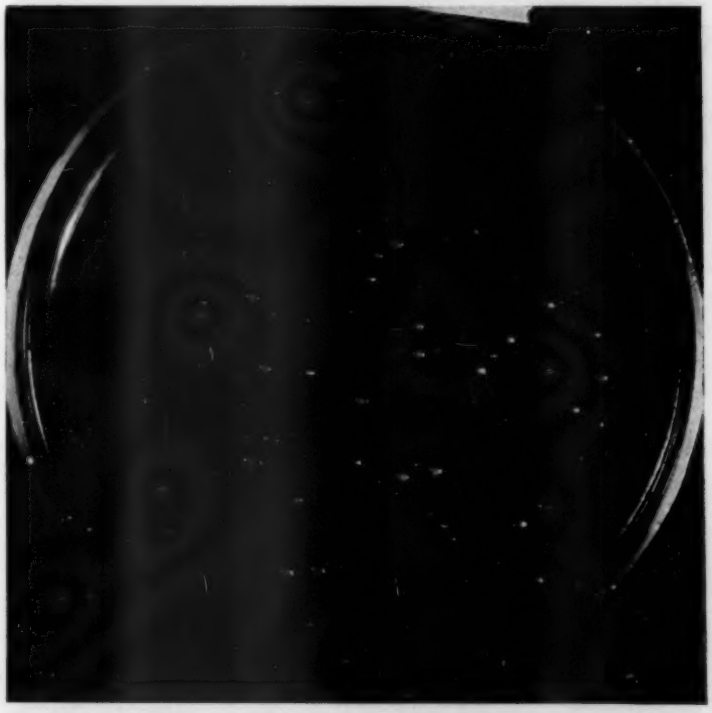

Fig. 4.—Urine before administration of mercurochrome-220 soluble: plate containing 1 c.c. of a 1:100,000 dilution of urine made thirty seconds after inoculation.

removed; dilutions of 1:100, 1:1,000, 1:10,000, 1:100,000 and 1:1,000,000 were made in 0.875 per cent. sodium chlorid solution; 1 c.c. of each dilution was added to melted p_H 7.6 beef infusion agar, and plates were poured. The results are graphically shown in Figures 4, 5, 6 and 7, which are photographs of the plates before and after administration of the drug.

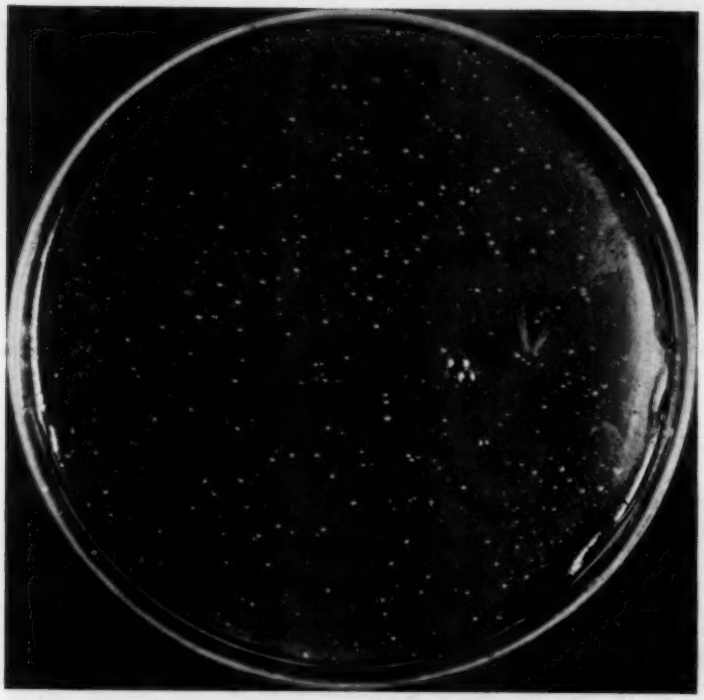

Fig. 5.—Urine before administration of mercurochrome-220 soluble: plate containing 1 c.c. of a 1: 100,000 dilution of urine, made twenty-four hours after inoculation, showing an increase in the number of organisms.

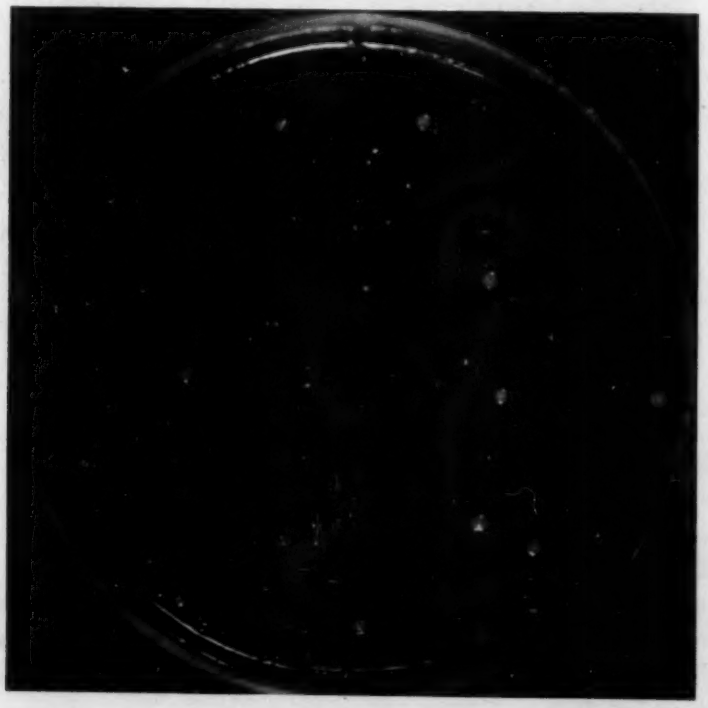

Fig. 6.—Urine one hour after administration of mercurochrome-220 soluble: plate containing 1 c.c. of a 1: 100,000 dilution of urine made thirty seconds after inoculation.

STERILIZING EFFECT IN RABBIT SYPHILIS

In connection with our studies of the action of other drugs on experimental syphilis of the rabbit,[8] three rabbits with well developed testicular infections with *Treponema pallidum* were given a course of intravenous injections of mercurochrome-220. Rabbit 210, with a lesion in the left scrotum, was given twenty-five injections, two weekly, of 2 mg. per kilogram of mercurochrome-220, treatment starting on the forty-ninth day after inoculation.[9] By the third injection, the induration was less; by the seventh injection, the lesion had completely resolved. The

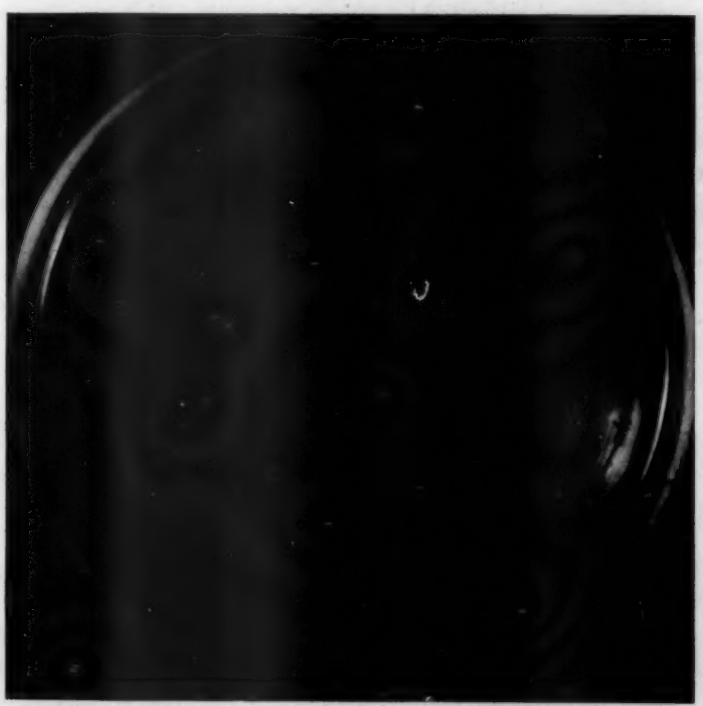

Fig. 7.—Urine one hour after administration of mercurochrome-220 soluble: plate containing 0.1 c.c. of urine made twenty-four hours after inoculation, showing no organisms.

animal was held without lesions for forty-seven days after the last injection, when a node transfer was done, which was negative during ninety days of observation.[10]

8. White, E. C.; Hill, Justina H.; Moore, J. E., and Young, H. H.: Flumerin—A New Mercurial for Intravenous Treatment of Syphilis, J. A. M. A. **79**:877-882 (Sept. 9) 1922.

9. Hill, Justina H., and Young, H. H.: Experimental Studies with Mercurials in Experimental Syphilis, J. A. M. A. **80**:1365-1369 (May 12) 1923.

10. Hill, J. H., and Young, H. H.: Ann. d. mal. vén. **19**:641, 1924. White, Hill, Moore and Young (Footnote 8). Hill and Young (Footnote 9).

A second animal, Rabbit 201, with nodular lesions in both testes, the right epididymis and right scrotum, received twenty-four injections of 2 mg. per kilogram of mercurochrome-220, beginning the forty-ninth day after inoculation. Resolution had started by the day of the third injection and was complete by the seventh dose. The animal was then held without lesions, a node transfer, made fifty-one days after the last injection, being negative during ninety days of observation.

A third, Rabbit 208, after receiving the same treatment with complete resolution of large bilateral testicular lesions by the fifteenth dose, relapsed twenty-eight days after the last injection. This rabbit was then given a second course of treatment, consisting of fifteen intravenous injections of 5 mg. per kilogram of mercurochrome-220, three weekly. Resolution of the testicular lesion began after the second dose. A node transfer, made sixty-eight days after the last dose, was negative during ninety days' observation.

To summarize, it is possible to drive a syphilitic infection from the lymphatics of rabbits with repeated injections of 2 mg. per kilogram of mercurochrome-220; in one case 5 mg. per kilogram was necessary. There was no abnormal variation of the phenolsulphonephthalein output during this treatment, the weights of the animals remaining about constant.

Piper,[11] suspending *Streptococcus hemolyticus* in defibrinated blood, found that a 1:8,000 dilution of mercurochrome-220 killed such a suspension in forty minutes. "In a 1:16,000 dilution, plates prepared at the end of one hour showed 2 colonies. Those prepared after this showed no growth."

ANTISEPTIC ACTION WHEN GIVEN BY MOUTH

In a study on the use of mercurochrome-220 soluble by mouth, we have administered it to animals and to patients in pills coated with phenyl salicylate,[12] and have shown definitely that the intestinal flora is modified and the bacterial content sufficiently reduced by such administration to justify further studies, not only of its effect in normal feces but also in intestinal infections, with the typhoid-dysentery group of bacilli, and, possibly, the pathogenic protozoa.

In a dosage of 900 mg. of mercurochrome-220 daily, the urine shows colorimetrically a dilution of between 1:15,000 and 1:40,000. At this strength, the urine is bacteriostatic. The stools become deeply stained, almost brick red in color, and the bacterial content may be greatly reduced.

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11. Piper, E. B.: Am. J. Obst. & Gynec. **4**:532 (Nov.) 1922.

12. Young, H. H.; Scott, W. W., and Hill, J. H.: J. Urol. **12**:237-249 (Sept.) 1924.

It seems evident that this method may be of value in combating local infections in the intestinal tract, and thus eliminating the cause of urinary infection. It seems probable that mercurochrome-220 administered by mouth may be of value in colitis and other diseases and infections of the intestinal tract, and for the preparatory treatment for gastro-intestinal operations. Further studies will be necessary before the limitations and possibilities of this method of treatment are fully determined.

BACTERICIDAL ACTION IN BILE IN TYPHOID CARRIERS

Studies have also been made by us in regard to action of mercurochrome-220 as a biliary antiseptic.[13] When a drainage tube was inserted into the gallbladder of a rabbit and then an intravenous injection of mercurochrome-220 given, it was found that the drug appeared in the bile about fifteen minutes after injection. It was present in bile after a single injection of 5 mg. per kilogram, in concentrations of from 1 : 5,000 to 1 : 50,000, as estimated by colorimetric comparisons of bile specimens from which the pigments were dissolved by Schlessinger's solution. The excretion of mercurochrome-220 in bile has also been studied by Rosenthal and White.[14]

It was also shown that mercurochrome-220 in vitro is actively bactericidal in a bile medium of exposure, killing *B. typhosus* Rawlings in one hour in a dilution of 1 : 1,000, in twenty-four hours in a dilution of 1 : 50,000. Similar killing strengths were found against the paratyphoid bacilli and *Vibrio comma.*

The bile obtained from rabbits after intravenous injection of mercurochrome-220 was found to be strongly bacteriostatic or bactericidal, in comparison to the heavy growth of organisms, *Bacillus coli* and *Staphylococcus aureus,* in bile specimens obtained before drug administration.

Moreover, it was possible to sterilize the bile of rabbits experimentally infected with *Bacillus typhosus,* by direct inoculation of the gallbladder. This curing of experimental carriers was accomplished with an intravenous injection of 5 mg. per kilogram and 3 mg. per kilogram, and with treatment for one week with two administrations daily of 7.5 mg. per kilogram by stomach tube. The experimental results clearly indicate the clinical trial of mercurochrome-220 in cholecystitis and chronic biliary typhoid carriers. In Case 7, here recorded, mercurochrome-220 appeared in the bile escaping from a biliary fistula.

13. Hill, J. H., and Scott, W. W.: An Experimental Study of Mercurochrome-220 Soluble as a Biliary Antiseptic, Arch. Int. Med. **35**:503 (April) 1925.

14. Rosenthal, S. M., and White, E. C.: J. Pharmacol. & Exper. Therap. **24**:265-288 (Nov.) 1924.

Reference should also be made to the most interesting experiments of Freeman and Hoppe [15] on the antiseptic action of the lung fluid after the intravenous administration of mercurochrome-220 to dogs. In a later article,[16] the same authors describe the following experiments:

A full grown rabbit was given 5 mg. of mercurochrome-220 per kilogram of body weight intravenously. Another rabbit of approximately the same weight, used for a control, received nothing. One hour later both animals were killed and the lungs from each rabbit were macerated and the fluid expressed from this was collected in separate sterile containers. The fluid from the lungs of the rabbit injected with mercurochrome was divided and inoculated in duplicate sets with the following bacteria: Pneumococci Types I, II, III, IV; *Streptococcus hemolyticus* and *Staphylococcus albus*. These sets were allowed to stand for fifteen minutes and one hour, respectively, then plated and incubated for twenty-four hours. The fluid from the control rabbit's lungs was treated in identically the same way. This experiment was repeated three times, using dogs as well as rabbits with similar results in all cases. The results of these experiments show that following the intravenous injection of mercurochrome fluids squeezed from the lungs are inhibitory to the growth of bacteria.

TABLE 2.—*Effect of Mercurochrome-220 Soluble on Growth of Bacteria in Fluids Squeezed from the Lungs (Hoppe and Freeman)*

Type of Bacteria	Control Serum Standing 15 Minutes	Mercurochrome-220 Serum Standing 15 Minutes	Control Serum Standing 1 Hour	Mercurochrome-220 Serum Standing 1 Hour
Pneumococcus Type I.....	48 colonies	Sterile	33 colonies	Sterile
Pneumococcus Type II.....	640 colonies	Sterile	34 colonies	Sterile
Pneumococcus Type III.....	29 colonies	2 colonies	250 colonies	Sterile
Pneumococcus Type IV.....	Too numerous to count	Sterile	63 colonies	14 colonies
Streptococcus hemolyticus....	13 colonies	5 colonies	15 colonies	7 colonies
Staphylococcus albus.....	1,072 colonies	536 colonies	1,072 colonies	9 colonies

Reference should also be made to the experimental studies of DeWitt [17] on tuberculosis; of Lancaster, Burnett and Gaus [18] on staphylococci, and of Piper [11] on streptococci.

CLINICAL EXPERIMENTS ON DRUGS AS LOCAL GERMICIDE

The laboratory experiments detailed at length above have been interspersed with clinical experiments in the usage of the drug in dis-

15. Freeman, W. T., and Hoppe, L. D.: Am. J. Dis. Child. **28**:310-321 (Sept.) 1924.

16. Hoppe, L. D., and Freeman, W. T.: The Treatment of Pneumonia in Children with Mercurochrome Intravenously, Tr. South. Med. Soc., 1924.

17. DeWitt, L. M.: Action of Mercurochrome-220 and of Mercurophen, J. A. M. A. **75**:1422 (Nov. 20) 1920; J. Infect. Dis. **30**:363 (April) 1922.

18. Lancaster, W. B.; Burnett, F. L., and Gaus, L. H.: Mercurochrome-220, Clinical and Laboratory Report on Its Use in Ophthalmology, J. A. M. A. **75**: 721 (Sept. 11) 1920.

eased and also in healthy subjects. This usage has verified the laboratory results and has shown that mercurochrome-220 is an antiseptic of great value for practical usage. Its use was first begun locally in the urinary tract, and it has been employed successfully in wounds and diseases in various parts of the body. An accumulated literature of considerable length testifies to its value in most of the special fields of medicine. These clinical experiments have shown that mercurochrome-220 approaches the ideal as an antiseptic in that it is highly germicidal, especially in the presence of tissue fluids, serum, urine, bile and intestinal contents, is relatively nontoxic and nonirritating, highly penetrating, a deep and lasting stain asserting its bactericidal action over a long period, and that it causes little or no injury to the vein in which it is injected in 1 per cent. solution or to organs of the body through which it is eliminated. Even in large doses, nothing more than a temporary albuminuria with a few casts, but no decrease in kidney function, is present. The lesions disappear rapidly and no permanent damage (as far as we can find) results following its intravenous usage.

USE OF MERCUROCHROME-220 AS AN INTRAVENOUS GERMICIDE

The first case that proved the value of mercurochrome-220 as an intravenous germicide was that of a woman who came to us with bilateral pyelonephritis due to *Bacillus lactis-aerogenes*. Within twenty-four hours after an intravenous injection of 5 mg. per kilogram, the urine was sterile and the patient cured. This is the first positive demonstration of a therapia sterilisans magna with mercurochrome-220 (Case 84).

The second case was that of an almost moribund man with general septicemia whose blood was sterilized within twelve hours by 34 c.c. of a 1 per cent. solution of mercurochrome-220 (Case 1).

The third case was that of a man having an extensive retroperitoneal infection that disappeared promptly after an injection of 27 c.c. of 1 per cent. solution (Case 80).

Since then we have treated and compiled from others many cases demonstrating the value of mercurochrome-220 in all manner of general, local and urinary infections and have recently presented a careful study of 210 cases.[19]

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19. Young, White and Swartz (Footnote 1). Young, H. H.: Tr. Am. Urol. A., May 21-29, 1923; J. Urol. **11**:19 (Jan.) 1924; Mercurochrome as An Intravenous Germicide, Tr. N. Y. State M. Soc., Buffalo, Oct. 4, 1923; Tr. South. M. A., Nov. 13, 1923; Tr. South. S. A., Dec. 11, 1923; Cure of Retroperitoneal and Perinephritic Infection by Intravenous Injections of Mercurochrome, Bull. Johns Hopkins Hosp. **35**:14-16 (Jan.) 1924. Young, H. H., and Hill, J. H.:, Treatment of Septicemia and Local Infections by Intravenous Injections of Mercurochrome-220 Soluble and Gentian Violet, J. A. M. A. **82**:669-675 (March 1) 1924. Young, H. H.: Cura

(Footnote 19 continued on next page)

CLINICAL REPORT OF CASES

The recent literature about mercurochrome-220 soluble has contained so many brief papers based on inaccurate and insufficient evidence, much of which has done serious injustice to this form of intravenous therapy, that it seems imperative for us to get together this exhaustive study of the subject. The work of this clinic has been described in numerous papers and reports before medical societies.[19] Laboratory reports from this clinic are mentioned in the first part of this paper.

Interesting papers have appeared from other clinics, among which may be mentioned the original paper of Piper,[11] who reported five cases in which he had used mercurochrome-220, but apparently with inconclusive results, as he stated.

> These cases are certainly not definitely conclusive that in mercurochrome-220 we have found a cure for blood stream infection. In a condition of this kind in which there is some focus of infection, if we kill the bacteria that are in the blood stream, the best we can hope for is that by so doing we can give the human organism a chance to cure itself.

Bunten reported two cases,[20] one of pneumonia and one of perirenal infection following operation "in which the use of mercurochrome-220 seemed, as far as the original pathological condition was concerned, to be satisfactory, although salivation proved very distressing for a time." He laid great stress on the reactions produced in these two cases. Another paper of interest was that of Whitman [21] who reported twelve cases of genito-urinary infections, all gonorrheal, in some of which he obtained remarkably quick results from the intravenous injections of mercurochrome-220. Another interesting report is that of Freeman and Hoppe [15] who reported twelve cases of pneumonia in children with really very remarkable results. In the same paper, very interesting experimental work previously referred to was given.

Next came a very brief paper by Bond and Barrier,[22] in which a case of typhoid fever treated by mercurochrome was briefly cited.

Footnote 19 continued—
delle infezioni generali e locali con iniezioni endovenose di mercurochrome, Bull. d. r. Accad. med. di Roma, April, 1924; Mercurochrome dans le traitment de septicemie, Faculté de médecine, Paris, May 16, 1924. Young, H. H., and Birkaug, K.: The Cure of Scarlet Fever Complicated with Erysipelas and Streptococcus Septicemia, J. A. M. A. **83**:492-494 (Aug. 16) 1924. Young, H. H.: The Cure of Infections—General, Local and Urinary—By Intravenous Injections of Mercurochrome-220, Surg., Gynec. & Obst., January, 1925.

20. Bunten, J. C.: Salivation Due to Intravenous Use of Mercurochrome, J. A. M. A. **82**:1443 (May 3) 1924.

21. Whitman, W. A.: Merurchrome-220 Soluble Intravenously in Chronic Gonorrhea and Complications, J. A. M. A. **82**:1914 (June 14) 1924.

22. Bond, S. P., and Barrier, L. F.: J. Arkansas M. Soc. **21**:71 (Sept.) 1924.

Another article of considerable interest was that by Hopkins,[23] in which twelve interesting clinical cases, some with remarkable results, are cited. This was followed by a discussion, much of which was based on meager observations and unscientific data, largely unfavorable to the use of mercurochrome intravenously. Lavandera[24] also reports four venereal cases, three chronic and one acute gonorrhea, in which negative results were secured and reactions stressed, and in the same journal Reed and Lum[25] presented cases, two of which showed quite satisfactory results. The latest article is that of Adams.[26]

These conflicting reports and personal communications received from various quarters in which the fear of reactions and of permanent serious injury to the kidneys and other organs has been voiced have impressed us with the necessity of making a complete compilation of all cases, good, bad and indifferent, favorable and unfavorable, so that a very comprehensive and thorough estimation of the value of this new method of combating infections may be made.

We are therefore presenting here a series of 211 cases that we have compiled from our clinic, from other clinics and from physicians here and abroad, who have at the expense of much effort sent us, with more or less detail, reports of clinical cases, laboratory findings and bedside charts. We have also culled from the literature practically all cases that have appeared on the subject, and have abstracted from them, in many instances at great length and in others more briefly where it was necessary to conserve space. These details have been classified, tabulated and studied quite exhaustively and the facts presented as fully as may be so that unprejudiced observers can formulate their own opinions.

It is needless to say that, in a series of cases so compiled and from so many sources, there is great variety in the length and detail of the reports. In many instances, one would have desired more complete clinical and laboratory data and more detailed notes, particularly on the bacteriology and other laboratory findings. While many of these cases will, therefore, be considered inconclusive, they are given in order that they may be taken along with those more fully presented so that readers may form from this survey an impression of the entire subject. Where possible, we have quoted the opinion of the physician making these reports, for in the last analysis he is in a better position to judge the effect of the drug than those of us who simply read the case histories. In presenting this great mass of material, we feel that it is abso-

23. Hopkins, F. S.: Boston M. & S. J. **191**:732-736 (Oct. 16) 1924.

24. Lavandera, M.: Mercurochrome Therapy in Four Cases of Gonorrhea and Their Complications, J. A. M. A. **83**:1682 (Nov. 22) 1924.

25. Reed, A. C., and Lum, D. D.: Toxic Results of Dye Treatment in Septicemia, J. A. M. A. **83**:1681 (Nov. 22) 1924.

26. Adams, D. S.: Boston M. & S. J. **191**:781 (Nov. 20) 1924.

lutely convincing of the great value of intravenous injections of mercurochrome-220 in a wide variety of infectious diseases. Some of the opinions expressed herein may be much too roseate and may, in the future, require revision but, making due allowance for the over-enthusiasm of the reporter and of the limited number of cases he may have studied, the great unanimity of the majority of observers over so wide an area is convincing evidence of the value of this new form of therapy and of the excellent results that have so often been obtained. In some cases, the observers seem thoroughly justified in speaking of the cure of patients that were practically moribund and supposedly beyond relief. The comment that the results were immediate and spectacular which has occasionally been made seems to have been justified by a few of the extraordinary cases contained in this compilation.

Owing to the mass of material on hand, it has been necessary to conserve space as much as possible consistent with a presentation of sufficient data for an accurate estimate of the effect of mercurochrome-220 given intravenously. This includes the reaction produced; the immediate and remote effect of the injections, general and local; the ultimate value of the drug in the given case when used alone, and when combined with other medication or surgical operation. Very desirable data have been missing in many of the reports. In other cases, it has been necessary to cut the case report short to conserve space. The opinions expressed in the case abstracts are those of the physician reporting the case to us.

FIFTY-SEVEN CASES OF SEPTICEMIA

TWO CASES OF URINARY ORIGIN

CASE 1.—*General septicemia due to Bacillus coli. Intravenous injection of 5 mg. per kilogram of mercurochrome-220. Recovery.*

H. A. D., a man, aged 44, weighing 68 kg., admitted, Dec. 30, 1922, complained of pain in the kidneys. The present illness was of three weeks' duration, following grip. The kidneys were very tender. Urinalysis showed considerable pus and *Bacillus coli-communior* on culture. Ureteral catheterization showed pus cells in a small amount from both kidneys, but no bacteria. On the following day, the pain in the right kidney became aggravated, and the patient was admitted to the Johns Hopkins Hospital, Jan. 2, 1923, with temperature 103.4 F., pulse 124, and in a very toxic condition. Examination showed muscle spasm and tenderness in the region of the right kidney, and the diagnosis of right pyelitis was made. On the following day, the patient's condition had become much worse; the temperature was still high, and the pulse very weak. The patient was irrational; there were purpuric eruptions on the neck, chest, abdomen and legs. Blood cultures showed a heavy growth of *Bacillus coli.* The patient was seen in consultation with the medical department, and the diagnosis of general septicemia was confirmed. The prognosis was apparently hopeless. The patient received 34 c.c. of a 1 per cent. solution of mercurochrome-220 (5 mg. per kilogram) in the vein of the arm. The temperature rose to 104 F. at midnight, but in six hours had dropped to 97. The patient became

rational in a few hours, and on the following morning his condition was marvelously transformed; the temperature was normal, and he said he felt quite well. A culture taken from the blood was sterile, and after that the patient continued to improve in strength. Subsequent cultures, January 5 and 8, also showed no growth. The patient was discharged from the hospital well, January 10. When seen in October, 1923, his condition was excellent; the urine was sterile by culture.

This is the first case to be recorded of cure of septicemia by the intravenous injection of mercurochrome-220.[27] The rapidity of restoration from imminent death to normal health was almost unbelievable.

CASE 2.—(Dr. F. B. Bowman[28]).—*Septicemia following urinary tract infection. Streptococcus hemolyticus from blood and urine.*

An intravenous injection of 5 mg. per kilogram of mercurochrome-220 was given. The temperature rapidly fell from 102 to normal, four days later. Twenty-five days later, another physician gave antistreptococcic serum. The

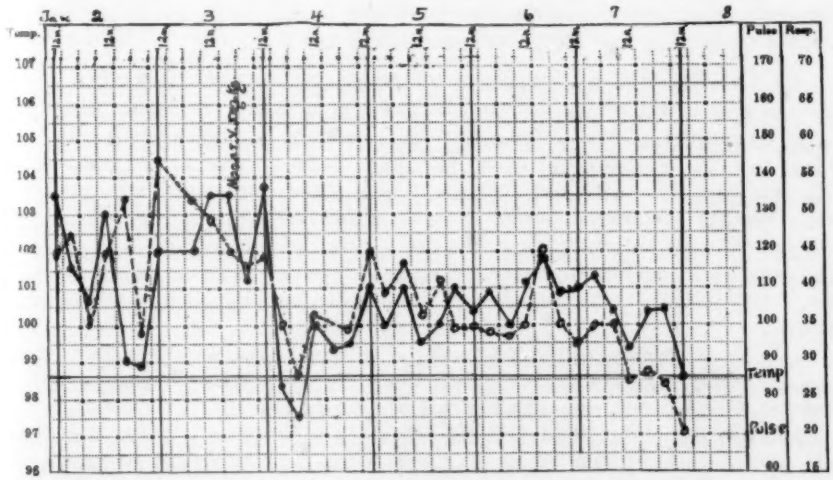

Fig. 8 (Case 1).—Pulse and temperature before and after intravenous injection of mercurochrome-220 soluble, 5 mg. per kilogram, in case of septicemia of urinary origin. Solid line, solid dot: temperature; broken line, open dot: pulse.

next day, the patient was given another injection of the serum and, the following day, died. Bowman stated that, personally, he thought that the serum was a mistake.

TWELVE CASES OF TRAUMATIC OR POSTOPERATIVE ORIGIN[29]

CASE 3.—*Staphylococcus septicemia, and extensive cellulitis following traumatism. Three intravenous injections of 1.7 mg. per kilogram of mercurochrome-220. Sterilization of blood and cure of local infection.*[30]

27. Young and Hill (Footnote 19, fifth reference).
28. Personal communication from Dr. F. B. Bowman, Hamilton, Ont.
29. Comparison should be made with Cases 58 and 165.

A man, aged 30, weighing 130 pounds (59 kg.) was injured in the right shoulder by a circular saw. The wound extended through the capsule of the joint and infection ensued. Following this, he had an extensive cellulitis of the shoulder region, which extended to the chest, beneath the pectoral muscles, and also down the arm and beneath the tissues of the back. Dr. W. L. Grantham of Asheville, N. C., saw him about two weeks after the accident, at which time his condition was very bad. The temperature was 104, and he was delirious. The infection of the chest, back, shoulder and arm was very extensive. A slide smear showed a staphylococcus infection of the wound. Blood cultures showed staphylococci in quantities. The patient weighed about 130 pounds (59 kg.), and he was given, intravenously, one injection of 10 c.c. of 1 per cent. solution of mercurochrome-220 (only 1.7 mg. per kilogram). Following this, he had a chill; the temperature, which was previously 104 F., went up to over 105, but in three hours fell to 102, and on the next day was 100, when he received another 10 c.c. of 1 per cent. mercurochrome-220 intravenously. On the following day, the temperature was normal. Two days later, the patient received a third dose (10 c.c. of 1 per cent. solution), and on the following day blood cultures were taken which proved to be negative, and the patient had an uninterrupted recovery. The cellulitis disappeared; the wounds healed completely, and the patient was discharged well.

CASE 4 (Kohlbry[30]).—*Streptococcus septicemia. Local abscesses. Five intravenous injections of mercurochrome-220 and gentian violet. Incisions. Recovery.*

A boy, aged 2 years, weighing 13 kg., admitted, July 19, had been circumcised ten days before admission; the wound became infected one week later and the glands of the neck became large. The temperature was 103. On examination, the infected circumcision wound was present; the throat was red; the tonsils were enlarged, suggesting an abscess; the glands on both sides of the neck were considerably enlarged, hard and did not fluctuate, and the lungs, heart and abdomen were negative. The diagnosis was infection of the cervical glands.

July 21, an incision was made and the abscess of the neck was drained; a large amount of pus was evacuated. July 26, an abscess of the hand had developed. The temperature had varied betwen 101 and 104.

July 26, the child was irrational. The temperature was 102.8; the white blood cells totaled 15,000. A blood culture grew a nonhemolytic streptococcus. An intravenous injection of 5 c.c. of 1 per cent. mercurochrome-220 was followed by no reaction. July 28, a second blood culture was positive following a second intravenous injection of 5 c.c. of 1 per cent. mercurochrome-220. July 29, a third intravenous injection of 4.5 c.c. of 1 per cent. mercurochrome-220 was given. July 30, a blood transfusion of 225 c.c. was followed by a severe reaction. The temperature was 105.6. August 1, after a fourth intravenous injection of 5 c.c. of 1 per cent. mercurochrome-220, the temperature was 105.6 and the abscess of the hand was fluctuating. August 2, the temperature was normal; there were several stools with blood and mucus. August 3, the child seemed considerably improved. August 4, a blood culture produced streptococcus and staphylococus. August 5, the temperature had risen to 103.6; there was evidence of abscess in the left knee and elbow and the white blood cells totaled 17,000. An intravenous injection of 7 c.c. of 0.5 per cent. gentian violet was administered.

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30. Personal communication from Dr. E. O. Kohlbry, Duluth Clinic, Duluth, Minn.

August 8, the left hip was infected. August 8, the fifth intravenous injection of 7 c.c. of 1 per cent. mercurochrome-220 was administered. August 12, the temperature was 102. Ten cubic centimeters of 0.5 per cent. gentian violet was given intravenously. The abscess of the arm was opened. August 13, the blood culture was negative. August 15, a blood transfusion of 250 c.c. was done. August 23, the patient was improved; the neck and arm wounds were healed; the hip was no longer swollen and there was some swelling of the knee. September 1, the temperature was normal; the patient was using the left arm well, and there was slight swelling of the knee. September 5, the patient was discharged from the hospital. The temperature had been practically normal since August 26. There was ultimate complete recovery.

CASE 5 (Roeder and Judd[31]).—*Septicemia following operation for cancer of breast. Staphylococcus albus. Two intravenous injections of 5 mg. per kilogram of mercurochrome-220. Recovery.*[30]

W. H. S., a white woman, aged 46, married, of marked adiposity, complained of bleeding from the left nipple over a period of one year. No mass was palpable, perhaps owing to the extreme adiposity. The left breast was removed by a Warren incision. No tumor mass was found at operation, but the pathologist discovered a nodule, 1 cm. in diameter, which was a definite carcinoma. The postoperative course was uneventful until the twentieth day when a small slough was trimmed from the flap, followed in twenty-four hours by a steady rise in temperature and pulse. Three days later, the temperature reached 105; the pulse was 140; the blood count totaled 22,000, and the patient presented a marked septic appearance. The blood culture carefully taken at this time showed *Staphylococcus albus,* which quite likely came from the trimming of the slough.

An intravenous injection of 30 c.c. of 1 per cent. mercurochrome-220, 5 mg. per kilogram, was given followed within one hour by a twenty minute chill, a rise in temperature to 106 and pulse to 150. In three hours, the temperature fell to 100.8 and the pulse to 90. In twelve hours, the clinical picture was markedly changed, although there was still some vomiting, with moderate salivation. General improvement was rapid, and the patient was discharged, seven days later, with a small, persisting sinus. Twenty-one days later, a typical erysipelatous infection developed around this sinus, extending over an area about 8 inches (20.3 cm.) in diameter.

Twenty-four hours after the onset of this infection, the patient had a temperature of 101.4 and pulse of 110. Local treatments of saturated magnesium sulphate were started immediately, but, twelve hours later, the temperature rose to 104, the pulse to 130, and there was extension of the erysipelatous margin. An intravenous injection of 30 c.c. of 1 per cent. mercurochrome-220 was given, followed within one-half hour by a chill, a temperature of 106.6 and pulse of 150. In twelve hours, the temperature had dropped to 100 and the pulse to 90. Within twenty-four hours, the erysipelas faded remarkably. On the second day following the mercurochrome therapy, the temperature reached normal and remained there, with an almost entire disappearance of the redness of the skin.

CASE 6 (Buddy[32]).—*Staphylococcic septicemia. Trauma. Intravenous injection of mercurochrome-220 and gentian violet. Recovery.*

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31. Personal communication from Drs. C. A. Roeder and W. H. Judd. Omaha, Neb.

32. Personal communication from Dr. E. P. Buddy, St. Louis, Mo.

A man, aged 58, broke his right thigh by falling from a scaffold. He did not void after the accident, and was catheterized for the second day. Three days following the catheterization, he had a chill followed by elevation of temperature, and from then on ran a typical septic course with positive staphylococci in the blood culture. The septic course continued from June 18 until July 24, when I saw him in consultation. He was desperately ill with a low blood pressure and rapid pulse, and his recovery was practically despaired of. Mercurochrome-220 in 1 per cent. solution was advised and given intravenously, followed by a severe reaction. The temperature remained normal for about five days, when it went up again. He was then given gentian violet. This caused improvement for another week, when the septic course again started. He was given another injection of mercurochrome-220, following which the blood culture remained sterile and the improvement continued. I saw him September 22; he was out and around and, aside from pus cells in the urine, he seemed in a very good condition.

CASE. 7 (Cassady[33]).—*Muliple fractures. General septicemia. Local abscesses of bones and joints. Sloughing of leg. Amputation. Administration of mercurochrome-220, gentian violet and crystal violet. Several operations for drainage; ultimate recovery.*

A woman, injured by an automobile, had dislocated the hip. There also were a chip off the acetabulum, a dislocated clavicle, a compound fracture of the mandible, and a compound fracture of the tibia. Five days later, an abscess developed in the jaw at the fracture site and was opened, and the leg showed signs of infection. Ten days after the accident, an abscess cavity was opened on the medial side of the tibia. Blood cultures showed *Streptococcus viridans* and a few staphylococci. A metastatic abscess developed in the gallbladder, which was opened and drained under gas and local anesthesia. Three transfusions were given.

A few days later, the ankle and foot began to swell on the median surface over the malleolus, and this was incised and drained, a culture showing *Streptococcus pyogenes.* Three weeks after the accident, both flexor and extensor tendons in the foot were sloughing, and opening and draining of the foot was necessary six times in four weeks. During the fourth week, a metastatic abscess developed in the dislocated hip which was drained, the culture showing pure *Streptococcus viridans.* Endocarditis had developed during the second week. After slight improvement, swelling, edema and abscess of the foot developed in the sixth week. Amputation of the foot was done. There was now a large abscess cavity between the ileum and the capsule of the joint and around the neck of the femur; the gallbladder and mandible abscess were still draining; the stump was edematous and infected, and the patient's condition was very critical.

On Dr. Young's advice, by long distance telephone, the patient was given an intravenous injection of 20 c.c. of 1 per cent. mercurochrome-220, 3 mg. per kilogram. The temperature was 100.6, pulse 132 and respiration 32 when the drug was given. Thirty minutes after the injection, the temperature was 96, pulse 166 and respiration 40, the pulse finally getting so weak that it could not be felt. Two hours after the injection, after a chill, the temperature was 103.5 and the pulse stronger. By morning, the temperature was 98.6; pulse 128; respiration 32, and the abdomen was soft and down to normal. She was decidedly better. She was voiding mercurochrome-220, and the gallbladder

33. Personal communication from Dr. J. V. Cassady, South Bend, Ind.

was draining mercurochrome. The real improvement dated from that time. The temperature, the next day, was 102 and the pulse 140 after dressings. One injection of 0.5 per cent. crystal violet, 40 c.c., and two injections of 1 per cent. gentian violet, 20 c.c., were then given, with no reaction. After the first injection, the hip began to granulate and the edema had nearly disappeared from the stump.

Dr. Cassady said that he felt that the mercurochrome-220, the crystal and the gentian violet really brought the patient out of a very critical condition, one in which her chances of recovery were practicaly nil. Since then the patient made some rapid strides in improvement of her general condition. The kidneys showed some damage from the infection; the urine was loaded with casts, and there were a few pus cells and a trace of albumin. There was slight puffiness of the eyes and slight edema of the ankles. The jaw was draining; the gallbladder was draining; the stump of the leg showed only slight infection, and was gradually granulating. The hip still had an abscess cavity around the joint capsule and discharged pus, the infection persisting; cultures showed streptococci with a few staphylococci. Roentgen-ray examination showed partial osteomyelitic destruction of the head of the femur and acetabulum, an active process.

August 15, the urine was of lower specific gravity, loaded with granular, epithelial and hyaline blood casts and with a trace of albumin but little pus. There was slight puffiness of the eyes and edema of the ankles. The white blood cells totaled 18,000; the jaw, gallbladder and hip and stump of the leg all drained pus. September 4, the patient was at home, the hip still draining; the gallbladder and jaw had stopped draining, and the leg stump was healed: the kidneys and heart were "fairly good." The temperature for the last two weeks was not over 100. The general condition was much improved; the appetite was good; the patient was sleeping well and gaining weight. November 9, the wounds were healed; the patient was in excellent condition, the hip ankylosed.

CASE 8 (Barnes[34]).—*Septicemia following infected hand. Staphylococcus aureus. Intravenous injections of mercurochrome-220 and gentian violet. Recovery still uncertain.*

An adult man cut or scratched the palmar surface of the first phalanx of his left thumb. Two or three days later, it began to swell and be painful. At this time, Dr. Barnes was called in to look at it, and found a small scratch about one-fourth inch (0.6 cm.) in length, slightly inflamed and suppurative. This was opened, compressed and soaked with hot boric acid three or four times daily, and instructions given not to use the hand. The hand improved for four or five days, when the patient struck the thumb three times in one day. It suddenly began to swell with lymphangitis, the swelling extending up the arm. Dr. Barnes then reopened the wound, and found a small pocket of pus, subcutaneously, over the flexor tendon of the second phalanx. *Staphylococcus aureus* was found in the pus. After the area was reincised, the patient, against warning, drove a Ford, using the hand considerably. The infection then increased in severity, a severe swelling of the hand and forearm ensuing, with a lymphangitis extending to the shoulder, accompanied by fever and leukocytosis.

In the meantime, he had been taken to the hospital and incisions made in the hand and forearm. No pus was found in the hand, but a pocket developed along

34. Personal communication from Dr. W. H. Barnes, Berkeley, Calif.

the vessels near the interosseous space near the elbow. Cultures showed *Staphylococcus aureus, Bacillus fluorescens* and a nonhemolytic streptococcus. Rabbit and guinea-pig inoculations showed that *B. fluorescens* was responsible for the severe edema which, at the end of five days, had advanced up the arm and down the thorax to the waistline. This was between April 13 and April 18. April 18, his condition seeming desperate, he was given 20 c.c. of a 1 per cent. solution of mercurochrome-220. April 19, he received 10 c.c. of 1 per cent., and April 20, 7 c.c. of 1 per cent. mercurochrome. April 21, the edema of the arm and thorax had reduced tremendously, but the circulation of the arm had become obstructed at the elbow; the hand and forearm were gangrenous, and amputation became necessary. The white blood cells totaled 45,000; the polymorphonuclears, 94. Amputation was done April 21. The white blood cells began to recede, as did the temperature and pulse. Cultures still showed the three organisms named. Staphylococci were cultured from the blood stream. The urine had continually shown albumin 2 plus, sugar 0, pus 3 plus, epithelium cells 1 plus, and casts 0.

Since April 21, the patient has had spells of improvement and spells of depression. Two transfusions have been given. He was given three intravenous injections of gentian violet, containing 300 mg., 200 mg. and 200 mg., respectively, two days apart. The blood stream is apparently sterile; no organisms have been found recently, though he still continues to run a rectal temperature of 101-103 F., with a white blood count of from 10,000 to 30,000, and from 72 to 85 per cent. polymorphonuclears. The arm stump is nearly well. He has complained of extreme pain in the left femur and knee when moved. Recently, he has developed considerable edema of both feet. There is a slight tenderness in the left kidney region, though no swelling can be made out at this time. His condition, although he has hung on so well, is not considered very favorable.

Case 9 (Janjigian[35]).—A patient developed septicemia after amputation of a leg. An intravenous injection of 5 mg. per kilogram of mercurochrome-220 was given twice. What was termed a "miraculous improvement" was noticed the next day, and all symptoms of septicemia disappeared. Other cases of septicemia (number not stated) were not cured.

Case 10 (Hall[36]).—A patient with sepsis following appendectomy was given an intravenous injection of 15 c.c. of mercurochrome-220. The temperature fell to normal. The white blood cells dropped from 12,000 to 5,000. Rapid recovery followed.

Case 11 (Colston[37]).—A boy, aged 6 years, with septicemia following vaccination had abscesses of the knee and elbow, which were later opened. An intravenous injection of 4 mg. per kilogram of mercurochrome-220 was given, with ultimate recovery.

Case 12 (Sica[38]).—A patient with postoperative septicemia and pleurisy had a septic temperature of 103.8. A blood culture produced *Staphylococcus aureus.* Two intravenous injections of mercurochrome, 15 c.c. and 10 c.c., were given. On the following day there were no chills and the patient was improved. A

35. Personal communication from Dr. R. R. Janjigian, Wilkes-Barre, Pa.

36. Report of Dr. E. P. Hall, Tarrant County, Texas, in Texas State M. J., May, 1924, p. 1924.

37. Personal communication from Dr. J. A. C. Colston, Baltimore.

38. Personal communication from Dr. Sica, St. Francis Hospital, Hartford, Conn.

blood culture was negative. The patient insisted on leaving the hospital. Pleurisy was present. Empyema developed. Drainage was done and 1 quart (liter) of pus removed. The patient died.

CASE 13 (Estes[39]).—In a case of septicemia cultures showed a hemolytic streptococcus following removal of the appendix and gallbladder. Intravenous injections of 0.5 per cent. gentian violet, 35 c.c. and 30 c.c., were given without reaction and without result. The blood culture increased in colonies. Twenty-eight cubic centimeters of gentian violet was given. As a final effort, the patient being moribund, an intravenous injection of 40 c.c. of 1 per cent. mercurochrome-220 (6.3 mg. per kilogram) was given. The patient died forty-eight hours later. Gentian violet was used because *Staphylococcus aureus* had been found in the abdominal wound.

CASE 14 (Roeder and Judd[21]).—A patient in extreme shock with the right arm torn off below the elbow had sepsis following amputation. The temperature was 104. An intravenous injection of 30 c.c. of 1 per cent. mercurochrome-220 was given. There was a mild reaction and slight improvement. Death followed forty-eight hours later.

SIX CASES OF THROAT INFECTION[40]

CASE 15 (Young and Birkhaug[41]).—*Scarlet fever. Streptococcus hemolyticus. Septicemia. Mercurochrome-220, 7.5 mg. kilogram. Recovery.*

A boy, aged 4 years, admitted, March 2, 1924, with scarlet fever, had marked enlargement of the tonsils and erysipelas. The temperature was 103; the pulse, 135. He was treated with Dochez' antistreptococcic scarlatinal serum without result. Cultures from the throat and blood cultures showed *Streptococcus hemolyticus.* March 7, at 11 p. m., the temperature had risen steadily to 106 F., and the pulse to 145. The drowsiness and delirium remained unchanged, and the erysipelas had extended over the face, about 2 cm. in all directions, during the last twenty-four hours. The child had vomited three times. The urine showed one plus albumin, with many white blood cells and a few granular casts. The blood examination revealed white blood cells 32,780, of which polymorphonuclears were 85 per cent.; polymorphonuclear eosinophils, 0; lymphocytes, 7 per cent., and myelocytes and transitionals, 8 per cent.

March 8, at 9 p. m., the temperature was again 105, the pulse 140, and respiration 37. There was no improvement in the general condition. The erysipelas had spread, markedly, behind the right ear and into the occipital region; the tenderness was acute, and the skin was strikingly hyperthemic. The glands at the angle of the jaw, on each side, were still much enlarged. The faucial ring was unchanged. The general condition was aggravated. The urine showed two plus albumin, many white blood cells and red blood cells and a few granular casts and bacteria. The blood culture was the same as that of March 6, *Streptococcus hemolyticus.* The blood examination, at 9:05 p. m., revealed white blood cells, 36,960. March 8, at 9:10 p. m., an intravenous injection of 15 c.c. of 1 per cent. mercurochrome-220, 7.5 mg. per kilogram, was given. The blood examination two hours later (11:08 p. m.) revealed white blood cells 22,900. There was no marked reaction as a result of the intravenous injection.

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39. Personal communication from Dr. W. L. Estes, Bethlehem, Pa.
40. Reference should also be made to Case 50.
41. Young and Birkhaug (Footnote 19, eighth reference).

March 9, the general condition of the patient had markedly improved. The delirium had entirely disappeared; the patient was mentally clear. The redness of the face was less intense, and there had been no untoward symptoms following the injection of mercurochrome-220; no nausea, vomiting or diarrhea were observed. The most striking feature was the complete sterilization of the blood as early as twelve hours after the injection of mercurochrome-220. There was a drop in the temperature from 105 to 101, within fifteen hours after the injection, and likewise in pulse rate from 140 to 98 within the same period. The white blood cells totaled 15,200. The patient made an uninterrupted recovery. The urine became clear, sterile and free from albumin and casts. By March 13, the appearance of the face and throat were practically normal. The cervical glands were not palpable. The white blood cells totaled 9,160. March 16, the condition was excellent. The throat, the urine and the temperature were normal. The patient was discharged.

CASE 16 (Morrison[42]).—*Septicemia. Streptococcus hemolyticus. Two intravenous injections of mercurochrome-220, 8 mg. per kilogram. Recovery.*

A boy, aged 6 years, weighing 44 pounds (20 kg.), was being treated at his home for a streptococcus sore throat so mild that it was difficult to keep him indoors. He was first seen, March 25, 1924. He seemed to improve steadily until the evening of March 28, when the temperature (by mouth) which had never been above 100 rose to 102, and he complained of being tired. At 6 a. m., March 29, he had a chill. The temperature rose to 104. The urine was turbid and showed pus and granular and epithelial casts. The leukocytosis was 22,600. A blood culture was reported, thirty-six hours later, as positive for *Streptococcus hemolyticus.*

The child had a second chill, March 30, at noon; the temperature, at 1 p. m., was 105. He was transferred to Memorial Hospital, March 30, and at 7 p. m., an intravenous injection of 8 mg. per kilogram of 1 per cent. mercurochrome-220 was given. There was a marked reaction, the temperature rising from 102 (rectal) to 105, and the patient being nauseated for several hours. By 8 a. m. of March 31, the temperature dropped to 99.2. The urinary findings were unchanged, and blood cultures taken March 31 were reported, April 1, as still positive for *Streptococcus hemolyticus,* and a second injection of mercurochrome-220, 8 mg. per kilogram, was given. The reaction from this was hardly noticeable. The temperature rose from 102.2 to 103, and there was little discomfort. By 8 a. m. April 2, the temperature was 99. The urine now showed no pus and only a few hyaline casts. A blood culture taken April 2 was reported as negative, April 3, but positive after forty-eight hours. April 4, an intravenous injection of 4 mg. per kilogram of mercurochrome-220 was made. Repeated blood examinations after this injection were negative. (The laboratory reported that the blood taken March 29 was completely hemolyzed in forty-eight hours. That taken March 31 required seventy-two hours before hemolysis was completed, while that taken April 2 was not entirely clear at the end of four days.) April 1, when the second injection was made, an endocarditis was suspected; this was confirmed, April 4, when the last injection was done. Having no data to go on, Dr. Morrison was apprehensive of the effect of mercurochrome-220 on this condition, but saw no ill effects. After a stormy convalescence, due to the cardiac affection and an acute nephritis, this patient returned home, May 1, and a recent examination showed him in excellent health (Oct. 18, 1924).

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42. Personal communication from Dr. James Morrison, 807 Church Street, Lynchburg, Va.

CASE 17 (Mervine[43]).—*Septicemia; endocarditis; laryngitis; streptococcus infection. Two intravenous injections of 1 per cent. mercurochrome-220, 4 mg. per kilogram. Recovery.*

A boy, aged 9, weighing 92 pounds (41.7 kg.) who one week before had been taken with laryngitis, Nov. 19, 1924, had a high temperature which reached 105 daily. The pulse was 148, respiration 48. Râles were heard in both lungs, and pleurisy was present. There was a heart murmur. The urine contained albumin and hyaline casts. There was marked laryngitis. He was steadily getting worse, and the condition seemed very desperate. His physician, Dr. G. D. Mervine, called us into consultation. Intravenous injection of 15 c.c. of 1 per cent. mercurochrome-220 was advised, with repetition the next day and two days later if required. Blood cultures also were requested. These were later reported negative, but cultures from the throat showed streptococci. A letter, Dec. 4, 1924, stated that the mercurochrome-220 had "worked like a charm." The temperature and pulse dropped and stayed down. A second dose had been given and the patient experienced no untoward results from the injections. He now seemed perfectly normal. He ate, slept and appeared well. Dr. Mervine felt that the two injections of mercurochrome-220 had saved his life. The temperature chart had shown a normal temperature, November 22, the pulse was 88, and respiration 24.

CASE 18 (Freeman[44]).—*Pneumococcus septicemia, Type IV. Intravenous injection of two doses, 5 and 7.5 mg. per kilogram, of mercurochrome-220. Recovery.*

A woman, aged 38, weighing 130 pounds (59 kg.) had been taken suddenly ill with sore throat, headache and high temperature, Feb. 16, 1924. Two days later she underwent an incomplete abortion, the third month of gestation. On the following day curettement was done. The temperature ranged from 97 to 104.5, with one or two chills each day. March 9, the fever and chills continued and the patient was at times delirious. A blood culture showed many colonies of pneumococcus, Type IV. March 12, an intravenous injection of 28 c.c. of 1 per cent. mercurochrome-220, 4.6 mg. per kilogram, was made. The temperature rose from 103 to 106. The pulse was 138-160. Twelve hours after injection the temperature was 97, the pulse 92. There were considerable vomiting and diarrhea for twenty-four hours. Forty hours after the first, a second injection of 35 c.c. of 1 per cent. mercurochrome-220, 5.8 mg. per kilogram, was given intravenously. The reaction was slight; there was no diarrhea. A blood culture the next day was reported sterile. March 17, three days after the second injection the patient was markedly improved. A blood culture was sterile; the white blood cells totaled 6,000. The subsequent course of the disease proved that no further treatment was necessary as the temperature and pulse dropped to normal, and the patient had an uneventful convalescence. Dr. Freeman was quite convinced that without the intravenous injection of mercurochrome-220 this patient would not have recovered.

CASE 19 (Trout and Groseclose[45]).—*Septicemia following tonsillitis and thrombosis of jugular vein. Intravenous injection of 16 c.c. of 1 per cent. mercurochrome-220. Recovery.*

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43. Personal communication from Dr. Graydone D. Mervine, 204 West Main Street, Lock Haven, Pa.

44. Personal communication from Dr. E. B. Freeman, 412 Cathedral Street, Baltimore.

45. Personal communication from Drs. H. H. Trout and A. M. Groseclose, Roanoke, Va.

May 26, a blood culture in this case showed gram-positive diplococci. May 28, a second blood culture gave the same results. May 29, the temperature was 104.8. The internal jugular vein was ligated and a lateral sinus opened. May 30, the temperature was 104.8. May 31, an intravenous injection of 16 mg. of 1 per cent. mercurochrome-220 was given. June 1, the temperature was 101; June 2, 99, and June 3, 99. The temperature became normal and remained practically normal, and the patient was discharged, June 9, in good condition.

In three other cases in which these physicians used mercurochrome-220, one a case of gun-shot wound, one of appendiceal abscess and one of a boy with septicemia, following abscess, the patients died.

CASE 20.—*Septicemia following maxillary abscess.*

A patient who had grown steadily worse and for whom all hope of recovery had been given up was given an intravenous injection of 25 c.c. of 1 per cent. mercurochrome-220. The temperature immediately dropped, and the general condition the next morning was improved. He was given another injection of mercurochrome-220, but the condition gradually grew worse, and the patient died of brain involvement a few days later.

TWO CASES OF EAR AND LATERAL SINUSES

CASE 21 (Schaub[46]).—*Septicemia following mastoid operation. Streptococcus. Intravenous injection of gentian violet and mercurochrome-220.*

A girl, aged 7, weighing 34 pounds (15.4 kg.) admitted to the hospital January 1, five days previously had had paracentesis done. On admission, a marked mastoiditis was present and an operation was carried out at once; the abscess was evacuated. The temperature remained septic. A blood culture was positive for streptococcus. Four days after the operation, both lungs became involved, complete consolidation ensuing.

For three weeks the temperature reached 104 or 105 daily. The condition was very grave. An intravenous injection of 10 c.c. of 0.25 per cent. gentian violet was given, followed by a drop of the temperature to normal. The next day the temperature was 105, and 25 c.c. of a 0.25 per cent. gentian violet solution was given intravenously. The temperature fell to 100. During the next four days the temperature was 103, 105 and 105.5. January 30, an intravenous injection of 7 c.c. of 1 per cent. mercurochrome-220, .5 mg. per kilogram, was given. The temperature fell to normal and remained there the next day. A blood culture was reported negative four days later. Subsequent blood cultures were negative. The temperature continued septic. The patient's emaciation was extreme, and her exhaustion profound. She was unable to turn in bed without assistance.

February 18, roentgen-ray examination showed a large pyothorax. Aspiration was done and later resection of a rib. At the same time, abscesses of the hip and knees were evacuated. A culture yielded staphylococcus. The temperature continued septic for a time, but the patient eventually made a complete recovery. At the last report the patient had been entirely well for a month.

As the blood culture, which contained streptococcus, did not become negative until after the mercurochrome-220 had been given, it seemed that the cure was due to mercurochrome-220. There were a few leukocytes and a trace of albumin in the urine, and there was intestinal disturbance after the injection of mercurochrome-220.

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46. Schaub, O. P.: Some Complications Following Operation for Simple Mastoiditis, Eye, Ear, Nose & Throat Monthly, May, 1924.

CASE 22 (Loudon[47]).—A girl, aged 6½ years, had septicemia and otitis media. Cultures yielded *Streptococcus hemolyticus*. The patient received four intravenous treatments with eusol, 20, 30, 40 and 45 c.c., over a period of eleven days with no effect. The temperature was 105, the pulse 140. The patient then received four intravenous injections of mercurochrome-220 at intervals of one, two and four days. The dosage was 12, 15 and 20 c.c. of 1 per cent. mercurochrome. There was no reaction. Blood cultures were still positive for *Streptococcus hemolyticus*. The patient died suddenly, May 13. Necropsy showed rupture of the aorta. The mercurochrome-220 diminished the daily variation in temperature from 5 to 2 degrees.

SIX CASES OF SEPTICEMIA FOLLOWING OSTEOMYELITIS OR ABSCESS

CASE 23 (Bourdeaux[48]).—*Septicemia following osteomyelitis. Mercurochrome-220, more than 6 mg. per kilogram. Recovery.*

Baby D., a boy, aged 3 years, was brought in with a large abscess of the right thigh following osteomyelitis of the right femur. The child was desperately sick, the temperature was high, 104 and above. The abscess was incised with free drainage, but the temperature continued to climb to nearly 106 and the patient was getting sicker. Intravenous injection of mercurochrome-220 was decided on as a last resort. Eight cubic centimeters of 1 per cent. solution was given with marvelous results. The temperature receded in a few hours to about normal. The pulse came down from 160 to 120, and it was felt that an early fatal termination had been averted by the use of mercurochrome-220. While the child had a slow convalescence, on account of successive joints becoming involved, he finally recovered. Another dose of mercurochrome-220 was administered several days later, when the temperature advanced to 103. The child made a satisfactory recovery.

CASE 24 (Sanmartin[49]).—*Septicemia following extensive furunculosis. Intravenous injection of mercurochrome-220. Recovery.*

Dr. Sanmartin described his illness in a letter as follows: "On March 1, in the city of Barranquilla, I contracted multiple furunculosis, which invaded all my body. This was accompanied by extensive glandular inflammation and suppuration of the glands of both groins, which were opened. But the fever continued with the presence of the phenomena of septicemia, with the formation of a deep abscess in the left hypogastric region. The fever continued with oscillation between 38.5 and 40 C. The pulse in the evening ranged from 110 to 140. There were rigors and frequent vomiting. Having read your article on the intravenous use of mercurochrome-220, I decided to take an injection of 20 c.c. of 1 per cent. mercurochrome-220. The reaction was fairly severe, but the temperature on the evening of the following day was only 38. The rigors and vomiting disappeared.

Three days later, I was given a second injection of 15 c.c., with less reaction. Six days later, the chills and pain in the abdominal region increased considerably. Two injections of mercurochrome-220 of 10 c.c. and 20 c.c. were given later which gave me a violent reaction lasting twelve hours; but the last injection produced a marvelous effect. ,After a few days, I was able to undertake, in a hydro-aeroplane, a voyage of 1,000 kilometers, and come to Bogota

47. Personal communication from Dr. Julian Loudon, Toronto.

48. Personal communication from Dr. T. B. Bourdeaux, Meridian, Miss.

49. Personal communication from Dr. Robert Sanmartin, Bogota, Colombia, S. A.

to be operated on for the hypogastric abscess. This was opened under general anesthesia, and today (June 19) I am completely well. I am convinced that the employment of these injections was my salvation. A culture taken from the abdominal abscess gave pure *Staphylococcus aureus*. On my advice mercurochrome-220 has been employed in two cases of puerperal sepsis and one of prostatitis, and in all three cases has given magnificent results" (translated).

CASE 25 (Weber [50]).—*Septicemia following osteomyelitis. Incision. Blood culture: Staphylococcus aureus.*

In this case, an intravenous injection of 4 mg. per kilogram of mercurochrome-220 was given. A blood culture was positive. Three blood transfusions were made. The leg was amputated. An intravenous injection of 12 c.c. of 1 per cent. gentian violet was given. Two more blood transfusions were made. An incision was made in the left hip. A blood culture was finally negative and recovery followed. The intravenous therapy was considered indispensable.

CASE 26 (Jenkins [51]).—*Multiple abscesses of liver. Septicemia. Multiple abscesses of joints and soft tissues. Numerous injections of mercurochrome-220 and gentian violet. No result. Death.*

A man, aged 30, weighing 150 pounds (68 kg.) had septicemia with multiple abscesses of the liver. A culture yielded staphylococcus. Five intravenous injections of 1 per cent. mercurochrome-220, 20, 20, 20, 16 and 20 c.c., respectively, and two injections of 20 c.c. of 0.5 per cent. gentian violet were given. There were multiple abscesses of the bones and joints. The treatment was ineffectual and the patient died.

CASE 27 (Reilly [52]).—The patient, aged 82, had sepsis following an abscess of the leg. Cultures yielded streptococcus and staphylococcus. An intravenous injection of 2 mg. per kilogram of mercurochrome was given. There was no reaction. The septic temperature continued. Objection by the family prevented further injections. The patient died ten days later.

CASE 28 (Colston [53]).—*Septicemia following operation for osteomyelitis. Blood culture: Staphylococcus aureus-hemolyticus.*

In this case an intravenous injection of 5 mg. per kilogram of mercurochrome-220 was given. There was no reaction. The blood culture still remained positive. Two days later, an intravenous injection of 5 mg. per kilogram of gentian violet was followed by no reaction. The patient died six days later.

TWENTY CASES OF PUERPERAL INFECTION

TWELVE SUCCESSFUL CASES

CASE 29 (Adams [26]).—*Puerperal septicemia. Pelvic abscess. Drainage. Intravenous injection of 30 c.c. of 1 per cent. mercurochrome-220. Blood culture: gonococcus and staphylococcus. Recovery.*

A girl, aged 16, who had had a miscarriage two years before, had had gonorrhea seven months before admission. A second miscarriage one month before had been followed by pelvic cellulitis. On admission, April 17, 1924, she had acute salpingitis and peritonitis. A mass in the right vault was punctured without

50. Personal communication from Dr. R. A. Weber, Baltimore.
51. Personal communication from Dr. W. I. Jenkins, Akron, Ohio.
52. Personal communication from Dr. J. L. Reilly, Snow Hill, Md.
53. Personal communication from Dr. J. A. C. Colston, Baltimore.

obtaining pus. The condition gradually became worse. The temperature ranged between 99 and 103. The pulse was 140. A second pelvic puncture was made, and a large abscessed cavity was drained. There was no growth from this pus at the end of three days. April 21, the white blood cells totaled 64,000. Drainage was temporarily beneficial. The abdomen became quite tense, and severe pain was noted over the entire abdomen and the right side of the chest. Multiple skin emboli in the form of small furuncles appeared over the back and limbs. These showed staphylococci by smear. A second blood culture showed gonococcus, and the third "mucoid staphylococcus."

The nineteenth day after admission the condition of the patient had reached a moribund stage. A massive right lobar pneumonia existed, and the abdomen was distended and rigid. She was delirious and cyanotic; the temperature was 102.2; the pulse, 160, and respiration, 44. As the process could not be overcome by operation and conservative means, as a last resort an intravenous injection of 30 c.c. of 1 per cent. mercurochrome-220 was given. This was without reaction. Twelve hours later the temperature was 99, the pulse 128, and respiration 30. An uneventful recovery followed. The chest condition cleared up within two days; the furuncles rapidly dried up and the only elevation of temperature reactions noted thereafter were when the patient began walking.

At present, six months after discharge from the hospital, the patient is entirely well. It is fair to give the credit of this recovery to intravenous therapy. The effect was rapid and obvious. The organisms affected were gonococcus and staphylococcus.

Case 30 (Comfort[54]).—*Puerperal septicemia. Blood culture: staphylococcus. Six intravenous injections of mercurochrome-220. Recovery.*

A woman, aged 25, weighing 130 pounds (59 kg.), was admitted to the hospital June 10, 1923, with labor pains every 10 minutes. The previous history was negative. The urine, blood and blood pressure were good. The patient was delivered five hours later. There was a normal birth; the placenta was expressed entire, and there was slight laceration of the perineum. The temperature was normal.

On the fourteenth day and the two following days, the temperature was normal, and the patient was allowed to sit in a chair. The seventeenth day began with chills and fever. A vaginal examination was negative. Both tubes, the ovaries, and the uterus were normal. The urine was negative. The sputum was negative for tuberculosis. The blood was negative for malaria and typhoid. July 12, the patient had a chill lasting forty minutes. The temperature was 106, pulse 160 and respiration 48. She complained of pain in the left inguinal region, with swelling of the left leg. A blood culture taken the following day showed pure staphylococcus. The leukocytes totaled 18,000; erythrocytes, 2,500,000. July 15, a consultation was called. The diagnosis was septic phlebitis of the femoral veins.

It was advised to give 1 per cent. mercurochrome-220, as the patient's temperature was between 104 and 106, and the pulse, 140-160. July 19, a first dose of 20 c.c. of mercurochrome-220, 3 mg. per kilogram, was injected in the vein of the patient's arm. There was a reaction in fifty minutes which lasted an hour. The patient was pulseless; heat and stimulation were applied. July 20, the temperature dropped to 101; the pulse was 140; the urine and stools were

54. Personal communication from Dr. J. B. Comfort, St. Francis Hospital, Hartford, Conn.

lightly colored. July 23, a second dose was given with the same result and reaction. July 25, the pulse was 120, the temperature 100.2, and respiration 38. July 28, the patient had another chill. The pulse was 160, the temperature 105.2, and respiration 48. It was decided to give mercurochrome-220 until a negative culture resulted. July 30, a third dose of 30 c.c. of 1 per cent. mercurochrome-220 was given intravenously and a reaction followed. August 2, a fourth dose of 30 c.c. was given. July 30, the temperature came down to 101; the pulse was 140 and respiration 32. August 6, a sixth and last dose was given. The patient complained of looseness of the teeth, slight bleeding of the gums and diarrhea.

August 8, a blood culture was negative; the red cells totaled 4,000,000; the leukocytes 12,000. August 10, the temperature was normal, respiration 24, and pulse 124. August 20, a blood culture was still negative; there was no rise in temperature, but the pulse, which was 130, was weak and rapid. Physical examination revealed an enlarged heart with a loss of snap to the second sound. The impression was that the patient had myocarditis resulting from infection. September 20, the patient had gained in weight and strength. The temperature was normal; the pulse, 100. October 20, the patient was allowed out of bed, but she became cyanosed and the pulse went up to 130. November 1, the patient was able to walk across the room. November 20, the patient was able to do her own housework and suffered no bad result, with the exception of swelling in the left leg.

Case 31 (Trout and Groseclose[55]).—*Puerperal septicemia. Blood culture: streptococcus; diplococcus. Two intravenous injections of mercurochrome-220. 5 mg. per kilogram. Recovery.*

Mrs. R. W., aged 24, weighing 95 pounds (43.1 mg.), February 24, came to full term pregnancy. Delivery was with forceps; there was a perineal tear. She was admitted to the hospital March 6, eleven days after delivery. The patient was extremely ill, the temperature being 102, the pulse 136, and respiration 30. She was immediately curetted and irrigated. Several small pieces of placenta were removed. March 8, the temperature was 103; pulse 153 and respiration 32. A blood culture showed nonhemolytic streptococci and pneumococci and a few gram-negative bacilli.

In the evening, the patient was extremely ill and it looked as if she would not live through the night. An intravenous injection of 5 mg. per kilogram of 2 per cent. mercurochrome-220 was given. No reaction followed. The next day the patient felt and looked better. March 9, an intravenous injection of 5 mg. per kilogram of 1 per cent. mercurochrome-220 was given. A blood culture on this day, after the first injection, was negative. The patient improved markedly but, March 11, a large pelvic abscess was opened and drained. March 18, the patient had developed empyema of the left side of the chest. Aspiration was done, 700 c.c. of pus being removed. March 19, the rib was resected and the left side of the chest drained. She then improved slowly, and left the hospital in good condition, May 12. A blood culture, March 16, was negative.

Case 32 (Trout and Groseclose[55]).—*Puerperal septicemia and pneumonia. Blood culture: streptococcus. Pleurisy with effusion. Intravenous injection of 5 mg. per kilogram of mercurochrome. Recovery.*

Mrs. D. B. H., aged 32, weighing 130 pounds (39 kg.), admitted Aug. 21, 1924, had been delivered, July 17, with forceps. Three weeks after delivery

55. Personal communication from Drs. H. H. Trout and A. M. Groseclose, Roanoke, Va.

there was pain in the chest. The patient was very ill; the temperature was 103.6; pulse 140, and respiration 20. The right lung showed marked impairment of the percussion note below the fourth rib. One hundred fifty cubic centimeters of thin yellow fluid was aspirated from the right pleural cavity. A blood culture, August 23, yielded streptococci and pneumococci. At 8:30 p. m., an intravenous injection of 5 mg. per kilogram mercurochrome-220 was given. There was a sharp reaction; the temperature was 105, the pulse 140, and respiration 32. The following morning the temperature was 98.6. The patient convalesced rapidly and was discharged well, September 27. The organisms in the blood culture and the fluid from the pleural cavity were pneumococci and probably nonhemolytic streptococci. The urine, which contained many cocci August 21, was sterile August 25.

Case 33 (Malone[56]).—*Puerperal septicemia. Six intravenous injections of mercurochrome-220. Recovery.*

Mrs. H., aged 20, a primipara, was delivered of a normal female child, April 4, 1924. April 8, the temperature was 99.4. April 10, there was a foul vaginal discharge, but no pain. The temperature was 99.8. April 11, the patient had several chills. The temperature was 105 at 7:30. The patient, who was cold and sweating, was very sick, being greatly prostrated and depressed. The diagnosis was puerperal sepsis. She was sent to the hospital.

At 3 p. m., an intravenous injection of 2.5 grains (0.16 gm.) of mercurochrome-220 in 20 c.c. of distilled water was given. The same dose was repeated six hours later. She was allowed to rest until 9:30 a. m., when another dose of 3 grains (0.19 gm.) of mercurochrome-220 was given intravenously. There was no reaction from these injections. At 3 o'clock the next morning the temperature was 102 and at 10 a. m., 101.6. At this time, another intravenous injection of mercurochrome-220 was given. At 3 p. m., the temperature was 103.8. At 5 p. m., another intravenous injection of 2.5 grains (0.16 gm.) of mercurochrome-220 and at 6 p. m., the temperature had dropped to 99. It remained there until 9 a. m. the next day, when it went up to 100. Another dose was then given, and at 12 noon the following day the temperature was subnormal, and at 3 p. m. 99. There were very slight reactions, stomatitis and diarrhea. The temperature became normal and remained so until the patient was discharged from the hospital on the fifth day, apparently completely cured.

Case 34 (Ober[57]).—*Puerperal septicemia. Intravenous injection of 4.5 grains (0.29 gm.) of mercurochrome-220. Recovery.*

A woman, aged 18, was examined Aug. 6, 1924, suffering from a threatened miscarriage with slow dribbling water and pains, but no flow of blood. Four days later she was delivered of a 3 month old dead fetus and adherent placenta. The placenta was so adherent that it was necessary to remove the patient to a hospital, where under anesthesia, it was removed, August 11. The temperature rose to 105, and on the following day remained about 104. The yellow bronziness of the skin, drowsiness, absence of lochial discharge, haggard appearance of the patient and the irrational statements, together with the continued high temperature and the increasing general malaise were a vivid picture of a very sick patient with septicemia. Several other physicians that examined her were certain of the diagnosis of blood stream infection, but no cultures were taken.

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56. Personal communication from Dr. H. B. Malone, Chester, S. C.
57. Personal communication from Dr. B. F. Ober, Latrobe, Pa.

August 14, the temperature was 104 and the condition unchanged. An intravenous injection of 4.5 grains (0.29 gm.) of mercurochrome-220 in 25 c.c. of distilled water (about 5 mg. per kilogram) was made. In an inconceivably short time, the temperature dropped to normal, around which it remained until the patient was dismissed from the hospital, August 24, in excellent condition. The next morning following the injection, I found the patient reading a book, and she said she was feeling fine. This case was remarkable because of the rapid and spontaneous improvement of the patient.

CASE 35 (Case [58]).—*General septicemia following abortion. Two intravenous injections of mercurochrome-220, 4 mg. per kilogram. Recovery.*

A woman, aged 23, married, with one child 3 years old, was admitted to the hospital in an extremely septic condition. The temperature was 104; pulse, 130, and respiration, 28. The patient stated that she had suffered a miscarriage three days before, and had no unusual symptoms until the morning of her

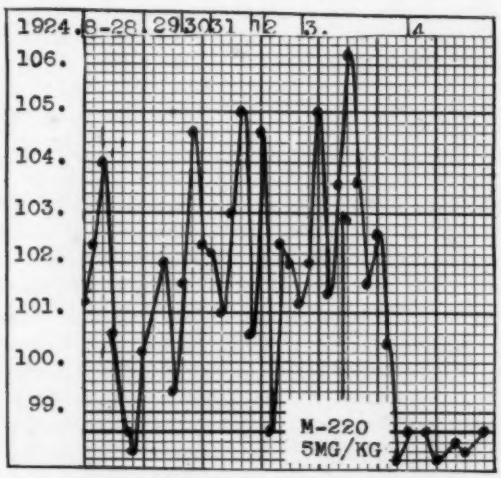

Fig. 9 (Case 36).—Temperature before and after intravenous injection of mercurochrome-220 soluble, 5 mg. per kilogram, in case of puerperal sepsis.

admission to the hospital, when she suffered pain in the lower part of the abdomen and extreme tenderness. She was nauseated, dizzy and very drowsy.

Examination disclosed a foul discharge from the cervix. A diagnosis of general septicemia following abortion was made. The patient was given 27 c.c. of 1 per cent. mercurochrome-220, 4.6 mg. per kilogram (the weight being 136 pounds [61.7 kg.]). The second day, the temperature began rising, and the patient was apparently becoming more septic. The patient was carried to the operating room, and a curettement with dull curets performed, a piece of catheter being removed. On the operating table, the patient was given an intravenous injection of 27 c.c. of 1 per cent. mercurochrome-220, 4.6 mg. per kilogram. Recovery was uneventful, and the patient left the hospital on the tenth day.

CASE 36 (Abraham [59]).—*Puerperal sepsis. One injection of mercurochrome-220, 5 mg. per kilogram. Recovery.*

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58. Personal communication from Dr. I. C. Case, Atlanta, Ga.
59. Personal communication from Dr. E. D. Abraham, Gibson, N. M.

A woman, aged 22, was admitted to St. Mary's Hospital, Gallup, N. M., Aug. 26, 1924, with a diagnosis of puerperal sepsis. Dr. Abraham was consulted, September 3, the twelfth day of illness. The daily temperature had varied from 98 to 105. She had received injections of antistreptococcus serum without benefit. She was very restless, appeared very toxic, and had a pulse of poor quality. In short, she was moribund. The temperature was 103. Mercurochrome-220 was advised, and the patient was given 5 mg. per kilogram in 1 per cent. solution intravenously. This was followed by a chill (Fig. 9). The temperature rose to 106.2, with a subsequent drop to normal in seven hours, at which time the patient expressed a desire for food. The temperature remained normal thereafter, and the patient was discharged, September 8, apparently well. A subsequent report stated that the patient was cured.

Case 37 (Case [60]).—A woman, aged 23, suffering from general septicemia following abortion, was extremely septic, the temperature being 104, the pulse 130. Two days later a fragment of catheter was removed by curettage. Two intravenous injections of mercurochrome-220, 4.5 mg. per kilogram were given. Recovery was uneventful, and the patient was discharged the tenth day well.

Case 38 (Davis [60]).—A woman (age and weight not given) with a history of abortion underwent curettement which was followed by chills and fever. She was admitted, Aug. 6, 1924, in a very septic condition. The temperature was high, and the condition continued to grow worse. The red blood cells totaled 3,350,000; white blood cells, 25,000, and the hemoglobin was 70 per cent. The urine examination showed albumin and pus cells, but no casts. Both forearms and arms were greatly swollen, and there was an abscess the size of an orange in the right axilla. The right thigh also was swollen. August 17, an intravenous injection of 20 c.c. of 1 per cent. mercurochrome-220 was given, which was repeated August 20.

Improvement after the first injection of mercurochrome-220 was very rapid, but the patient was given a third intravenous injection of mercurochrome-220 and, August 26, an abscess of one forearm was incised. The incision was about one-fourth inch (0.6 cm.) long, which was very small for an abscess of the size. As a rule, an incision about 4 inches (10.1 cm.) long is made. The patient recovered very rapidly. The swelling in the axilla had begun to disappear after the first injection of mercurochrome-220, and had almost entirely disappeared after the incision in the forearm. The patient was discharged, August 31, in excellent condition and apparently completely cured.

Case 39 (Davis [60]).—A woman (age and weight not stated), delivered of a baby, September 24, developed fever and, September 30, had a temperature of 105. The condition was so serious that it was thought the patient would not live. An intravenous injection of 20 c.c. of mercurochrome-220 was given. The temperature dropped in two days to 99.4 and then rose. October 2, mercurochrome-220 (dose not stated) was given intravenously and, October 6, a third dose. A later pelvic abscess was discovered, and opened by way of the vagina. The temperature dropped after the first injection of mercurochrome-220 from 105 to 99.4. It had looked as if the patient would not live, but from that time on there was no doubt of her recovery.

Case 40 (Case [60]).—A woman, aged 32, weighing 135 pounds (61.2 kg.), was admitted with temperature 104, pulse 140 and respiration 30, complaining of pain and soreness in the lower part of the abdomen. She had a history of

60. Personal communication from Dr. C. R. Davis, Detroit, Mich.

miscarriage five days previously. Examination disclosed pus exuding from the cervix. The patient was carried to the operating room and curettement performed with a dull curet. While on the operating table, the patient was given 37 c.c. of 1 per cent. solution of mercurochrome-220, 5 mg. per kilogram. The patient made an uneventful recovery, and was discharged on the tenth day.

FOUR PUERPERAL CASES IN WHICH EFFECT OF MERCUROCHROME-220 WAS DOUBTFUL

CASE 41 (Dr. Bowman[28]).—A woman, aged 27, following abortion developed severe septicemia. She was given an intravenous injection of mercurochrome-220, 7 mg. per kilogram. The reaction was marked. There were vomiting and typical symptoms of mercurialism, which were controlled by opium. After the reaction, the temperature became normal, and the patient left the hospital well, with the exception of moderate anemia. Dr. Bowman said that he did not know whether he should call this a cure by mercurochrome-220, but the symptoms improved and the patient went home well on the road to recovery.

CASE 42 (Loudon[47]).—*Puerperal septicemia. Intravenous injection of 20 c.c. of 1 per cent. mercurochrome-220, 4.6 mg. per kilogram. Recovery.*

A woman, aged 28, weighing 100 pounds (45.4 kg.) had puerperal septicemia. The white blood cells totaled 28,000. A blood culture was sterile. She had developed chills and fever on the third day after delivery. An intravenous injection of 20 c.c. of 1 per cent. mercurochrome-220, 4.6 mg. per kilogram, was given. There was no reaction. The patient got better, and was discharged within two weeks. The effect of the mercurochrome-220 was doubtful.

CASE 43 (Piper[11]).—*Puerperal septicemia. Streptococcus hemolyticus.*

The patient was treated with mercurochrome-220 (amount not stated) with slight reaction. Antistreptococcic serum also was given. Eventfully the condition localized as a cellulitic phlegmasia of the lower extremity, which was opened and drained, but the patient made a good recovery. Whether the mercurochrome-220 in this case was of any value cannot be determined.

CASE 44 (Piper[11]).—A woman had puerperal sepsis and thrombophlebitis of the lower extremities. A blood culture yielded *Streptococcus hemolyticus.* She was given mercurochrome-220. One week later, a blood culture was negative. Subsequently, she was given a second dose. She appeared to be better. Following this, she made a complete recovery.

Dr. Piper stated that this or his other cases certainly were not definitely conclusive that in mercurochrome-220 a cure for blood stream infection has been found. In a condition of this kind, in which there is some focus of infection, if the bacteria in the blood stream are killed, the best that can be said is that the human organism is given a chance to cure itself, he said.

FOUR PUERPERAL CASES IN WHICH MERCUROCHROME TREATMENT RESULTED IN FAILURE

CASE 45 (Hunt[61]).—*Puerperal septicemia. Pericarditis. Multiple focal abscess. Streptococcus hemolyticus. Intravenous injections of 45 c.c. and 25 c.c. of 0.5 per cent. mercurochrome-220. Did not recover.*

A woman, aged 37, weighing 125 pounds (56.7 kg.), admitted Feb. 22, 1924, had puerperal sepsis following abortion. February 25, the placenta was removed

61. Personal communication from Dr. Ernest L. Hunt, City Hospital, Worcester, Mass.

and blunt curettage done. February 28, the temperature was 103.4. February 29, a blood culture showed streptococcus hemolyticus. The white blood cells totaled 11,000. March 3, there was no improvement. There were a soft systolic murmur and râles in the lungs. An intravenous injection of 45 c.c. of 0.5 per cent. mercurochrome-220, 4 mg. per kilogram, was given. The reaction was pronounced, the eyelids were edematous and there were frequent stools and vomiting.

March 7, the specific gravity of the urine was 1.011; there was the slightest possible trace of albumin; there were no casts, but many white blood cells. An intravenous injection of 25 c.c. of mercurochrome-220 was given. This was followed by frequent bowel movements. The patient became comatose. March 11, she expired at 1:30 a. m.

Necropsy showed septic endometritis, septic pericarditis, general septicemia, multiple septic infarcts of the spleen and kidneys and acute nephritis. Chemical study of the kidneys showed a trace of mercury. In Dr. Hunt's opinion, they showed both focal and toxic degenerative nephritis.

CASE 46 (Lanier[62]).—The patient had puerperal septicemia. The temperature was 104; the white blood cells totaled 23,000. Five daily injections of 10 c.c. of 1 per cent. mercurochrome-220 were given. The blood was sterilized. Two more injections of mercurochrome-220 were given. The patient died of pulmonary embolism.

CASE 47 (Faulkingham[63]).—The patient had puerperal septicemia. A blood culture yielded *Streptococcus hemolyticus.* An intravenous injection of mercurochrome-220 was given. There was no reaction. A blood culture twelve hours later was positive. The patient died.

CASE 48 (Piper[11]).—The patient had puerperal septicemia. A blood culture yielded *Streptococcus viridans.* A dose of mercurochrome-220 (amount not stated) was given. Eventually the patient died.

SEVEN CASES OF SEPTICEMIA WITH ENDOCARDITIS[64]

CASE 49 (Bowman[28]).—*General Streptococcus hemolyticus septicemia following endocarditis. Three doses of mercurochrome-220, 5 mg. per kilogram. Recovery.*

A woman, aged 22, entered the hospital in a very serious condition, two consultants pronouncing her case hopeless. There was a rough, blowing aortic murmur; the temperature ranged from 101 to 103; the pulse, which was irregular, was 120. The patient had periods of cyanosis, and swollen, painful joints. A blood culture yielded *Streptococcus hemolyticus.* The patient was given three doses of mercurochrome-220, 5 mg. per kilogram. The temperature became normal, the pain and swelling left the joints, and a blood culture became negative. The patient left the hospital in two weeks quite well except for a soft blowing murmur in the aortic region. When last heard from, the patient was well, dancing and exercising.

Dr. Bowman was convinced that mercurochrome-220 had saved this girl's life.

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62. Personal communication from Dr. L. F. Lanier, Rocky Ford, Ga.
63. Personal communication from Dr. R. Faulkingham, New Brunswick, N. J.
64. Reference should be made to Cases 7 and 17.

CASE 50 (Emmett[65]).—*Endomyocarditis following acute mastoiditis and sinus thrombosis. Staphylococcus. Intravenous injection of 15 c.c. of 1 per cent. mercurochrome-220. Recovery with complete disappearance of heart lesion.*

F. C., aged 13, admitted March 14, 1924, had had tonsillitis two years and otitis media one year before. He had had a mastoid operation and ligature of a lateral sinus one month before. Following this he had severe chills, night sweats and a septic temperature. The diagnosis was septic endocarditis. Roentgen-ray examination showed the heart enlarged in all diameters. The systolic blood pressure was 110, diastolic 70. The white blood cells totaled 14,200; the red blood cells, 4,800,000. Hemoglobin was 75 per cent. The Wassermann reaction was negative.

March 18, the temperature was 101. The aggravated condition was diagnosed endocarditis. He had a high temperature, the pulse being 130. The heart apparently had a malignant infection. The initial infection was staphylococcus.

The results of our researches led Dr. Emmett to use mercurochrome-220. The patient received 15 c.c. of 1 per cent. solution. The temperature dropped to normal; the heart rate slowed down to normal and during the month that he remained in the hospital convalescing, he gained 13 pounds (5.9 kg.).

Dr. Emmett stated that the heart infection entirely cleared up, the patient having no cardiac symptoms. April 1, there was still some cardiac enlargement and a mitral systolic murmur. The heart sounds improved in quality and rhythm.

April 8, the patient had gained 11 points (5 mg.). The pulse was good, the temperature normal.

There was marked improvement. April 10, the patient was discharged, his condition good. In November the boy appeared healthy, rode a bicycle, played ball and had no heart symptoms. He had good color. The heart was 10 cm. from the midsternal line. The rate was 80. There was a soft, distant systolic murmur.

CASE 51 (Palmer[66]).—*Septicemia and endocarditis. Nonhemolytic streptococcus. Seven injections of mercurochrome-220 from 4 to 7 mg. per kilogram.*

A woman, aged 33, weighing 58 kg., had endocarditis. A blood culture yielded nonhemolytic streptococcus. Sept. 5, 1924, an intravenous injection of mercurochrome-220, 3 mg. per kilogram, was given. September 8, an injection of 4 mg. per kilogram and, September 15, an injection of 5 mg. per kilogram. The temperature fell gradually but steadily. The patient showed some improvement clinically. A blood culture was still positive. September 27, an intravenous injection of mercurochrome, 6 mg. per kilogram, was given. There was a severe reaction. October 6, 7 mg. per kilogram was given. There was a very severe reaction. The gums became sore; the blood count was still positive. October 13, 7 mg. per kilogram was given. There was a very severe reaction, but a total lack of effect on the blood culture. November 10, the temperature had risen slightly after the stopping of the mercurochrome-220. It was then 102 in the afternoon. A colony count was 16 per cubic centimeter. The patient was failing slowly.

The following case is cited to show efforts that have been used in a special case that was continually resistant to treatment. As the case was

65. Personal communication from Dr. F. Arthur Emmett, St. Francis Hospital, Hartford, Conn.

66. Personal communication from Dr. Walter W. Palmer, Presbyterian Hospital, New York City.

prononunced absolutely hopeless by the medical consultants, we felt that we were justified in trying one germicide after another intravenously in the hope that something would be beneficial, but, unfortunately, all efforts were unavailing. Table 3 is interesting as showing the effect of various chemicals used and the reactions produced.

CASE 52.—*Streptococcus viridans endocarditis and septicemia. Intravenous injections of mercurochrome-220, gentian violet, neoarsphenamin, sodium cacodylate and anilin green. Result, negative. Death.*

A man, aged 27 years, admitted Dec. 22, 1923, had a history of four attacks of rheumatism during the last twelve years. He was subjectively well until one month previous to admission, when he began to have nightly chills and fever. He became unable to walk because of painful ankles. The heart was enlarged with presystolic and systolic murmurs. Blood cultures showed *Streptococcus viridans.* A white blood count totaled 7,600. The temperature was 100, pulse 110 and respiration 28. The urine contained albumin, casts, red blood cells and cocci. The diagnosis was endocarditis and septicemia and, as medical consultants considered the case hopeless, it was decided to try almost every known form of intravenous therapy with the hope of possibly effecting a sterilization. The intravenous treatment and results are shown in Table 3. The hemoglobin was 65 per cent. on admission and, January 17, was 75 per cent. The patient died, April 6, 1924.

TABLE 3.—*Results of Treatment in Case 52*

Date	Condition Before Treatment	Intravenous Treatments	Blood Cultures No. Colonies per C.c. Streptococcus Viridans		Reactions
			Before	Next Day	
Admission	Blood culture: Streptococcus viridans	.....	..	..	.....
12/22/23	Urine: albumin, casts, white blood cells, cocci				
12/24/23	White blood cells 7,600, red blood cells 3,720,000	Mercurochrome-220, 5 mg. per kilogram	140	30	Temperature rose from 100 to 102; temperature normal 48 hours; felt better
12/26/23	Temperature 99.8 F., white blood cells 7,500	Gentian violet, 8 mg. per kilogram	85	150	Slight increase in temperature; white blood cells dropped to 4,200
12/30/23	White blood cells 3,500, red blood cells 3,550,000	750 c.c. citrated blood	100	65	Chill; blood count 3 days later: white blood cells 6,200; hemoglobin 78%; red blood cells 4,950,000
1/ 2/24	White blood cells 6,500, urine culture: cocci	Neoarsphenamin, 0.9 gm.	60	25	No reaction; urine sterile
1/ 3/24	White blood cells 6,300, urine: no cocci	Neoarsphenamin, 0.9 gm.	..	..	Urine: no casts, no cocci, trace of albumin
1/ 4/24	Little weaker, white blood cells 8,200	Mercurochrome-220, 8 mg. per kilogram	70	40	Slight chill; urine: few red blood cells
1/ 5/24	Temperature 100 F., white blood cells, 11,500	Neoarsphenamin, 0.9 gm.	70	Contaminated	No reaction; urine: few casts, red blood cells +
1/ 6/24	White blood cells 8,200	Mercurochrome-220, 5 mg. per kilogram	40	..	Constricted feeling across chest; gums sore
1/ 8/24	White blood cells 7,800, red blood cells 4,800,000	500 c.c. citrated blood	Not given	Not given	Slightly chilly
1/10/24	Slowly becoming weaker	Neoarsphenamin, 0.9 gm.	160	..	No reaction; urine: many casts; red blood cells +
1/11/24	Weaker.....	Sodium cacodylate, 300 mg. given intramuscularly	280	..	No reaction
1/17/24	White blood cells 8,800, hemoglobin 75%	Anilin green, 4 mg. per kilogram + 2 mg. per kilogram	250	300	Little pain over heart; urine: unchanged

CASE 53 (Adams,[26] Case 5).—*Acute mitral endocarditis. Intravenous injection of 40 c.c. of 1 per cent. mercurochrome-220.*

A woman, aged 42, whose blood culture was negative, was given an intravenous injection of 40 c.c. of 1 per cent. mercurochrome-220. She had severe diarrhea and reaction from the injection. She died one week later. Necropsy failed to disclose any mercurial effects on either the kidneys or the intestinal tract.

CASE 54 (Reed and Lum[25]).—A man, aged 24, had endocarditis. A blood culture yielded *Streptococcus viridans.* An intravenous injection of 30 c.c. of 1 per cent. mercurochrome was given, and the same dose on the following day. Dysentery resulted and there was no improvement. The patient died.

CASE 55 (Reed and Lum[25]).—A man, aged 45, had endocarditis. A blood culture yielded streptococcus. An intravenous injection of 38 c.c. of 1 per cent. mercurochrome was given the first day; the third day, 40 c.c., and the seventh day, 45 c.c. There was no improvement. The patient died.

TWO CASES OF SEPTICEMIA IN WHICH FOCUS OF INFECTION WAS UNCERTAIN

CASE 56 (Bowman[28]).—*Septicemia due to Streptococcus hemolyticus. Three intravenous injections of 5 mg. per kilogram of mercurochrome-220. Recovery.*

A girl, aged 9, entered the hospital with a temperature of 102, pulse 140, and respiration 20, having been sick several days with chills and fever. No focus of infection could be found. The second day the temperature was 106 in the evening, 99 in the morning. For three days there was a typical "saw" chart. A blood culture yielded *Streptococcus hemolyticus.* Three intravenous injections of 1 per cent. mercurochrome-220, 5 mg. per kilogram, were given. The temperature became normal, a blood culture was negative, and the patient was discharged apparently perfectly well. Although no focus was found in the mastoid, kidneys, throat or other sites, definite septicemia was present and was cured by mercurochrome-220.

CASE 57 (Adams,[26] Case 3).—*Chronic sepsis. Moribund patient. Intravenous injection of 40 c.c. of 1 per cent. mercurochrome-220. No effect. Death.*

A woman, aged 26, admitted May 6, 1924, had rheumatic fever of three month's duration. She was a very ill woman. She apparently was toxic. No foci were found. As a last resort, an intravenous injection of 40 c.c. of 1 per cent. mercurochrome-220 was given. There was no reaction and no effect was noted. The patient died six hours later.

ANALYSIS OF RESULTS IN SEPTICEMIA CASES

Analyzing the failures, we find that in Cases 14, 20 and 57 the patients were practically moribund when treated. Five cases, Cases 51 to 55, were of endocarditis due to a streptococcus, two recognized as *Streptococcus viridans,* notoriously resistant to all therapy. The three others also may have been *Streptococcus viridans.* In two cases with streptococcus endocarditis (Cases 49 and 50), the patient did, however, recover, and in one case of *Streptococcus viridans* endocarditis, Case 7, the patient also recovered.

In Cases 2, 13, 22, 26, 27, 28 and 45, which ended fatally, three of the patients received only one injection each, two received two injections of small dosage, and two received three of moderate size. In none of these eight cases did the patient receive two injections of 5 mg. per kilogram. It seems fair to state, therefore, that either the treatment was inaugurated too late or was not as vigorous as was given in the successful cases cited in Table.[4]

TABLE 4.—*Summary of Twenty-Four Cases of Septicemia All Said to Be "Cured" by Intravenous Injection of Mercurochrome-220*

Case	Age	Conditions in Addition to Septicemia	Blood Culture	Mercurochrome-220	
				No. of Doses	Milligrams per Kilogram
1	40	Pyelonephritis	Bacillus coli	1	5
3	30	Traumatic cellulitis	Staphylococcus	3	1.7, 1.7, 1.7
4	2	Tonsillitis; abscess	Streptococcus	5	4, 3, 4, 4, 6
5	46	Postoperative condition	Staphylococcus albus	2	5, 5
6	58	Traumatic cystitis	Staphylococcus	2	5 (?), 5 (?)
7	?	Traumatic osteomyelitis	Streptococcus viridans, staphylococcus	1	5
8	?	Infected hand cellulitis	Staphylococcus aureus	3	3, 2, 1
15	4	Scarlet fever; tonsillitis; adenitis	Streptococcus hemolyticus	1	7.5
16	6	Pharyngitis	Streptococcus hemolyticus	2	8, 8
18	38	Puerperal sepsis; pharyngitis	Pneumococcus IV	2	5, 7.5
19	..	Tonsillitis; phlebitis	Diplococcus	1	5 (approx.)
21	7	Mastoiditis	Streptococcus	1	5
23	3	Osteomyelitis; abscess	Staphylococcus ?	2	6 ?
24	40	Furunculosis; abscess of groin	Staphylococcus aureus	4	4 (?), 3, 2, 4
29	16	Pelvic abscess; furunculosis	Staphylococcus, gonococcus	1	5
30	25	Puerperal infection	Staphylococcus	6	3, 3, 5, 5, 5, 5
31	24	Puerperal infection	Streptococcus pneumococcus	2	5, 5
32	32	Puerperal infection and pneumonia	Streptococcus pneumococcus	1	5
33	20	Puerperal infection	Streptococcus ?	6	3, 4, 3, ?, ?, ?
34	18	Puerperal infection	Streptococcus ?	1	5 (?) approx.
35	23	Puerperal infection	Streptococcus ?	2	4.6, 4.6
36	22	Puerperal infection	Streptococcus ?	1	5
49	22	Endocarditis; arthritis	Streptococcus hemolyticus	3	5
56	9	No focus found	Streptococcus hemolyticus	1	5

It seems evident, therefore, that in septicemias doses of 5 mg. per kilogram should be used and repeated as often as necessary or as possible.

Summary: Twenty-four cases; all recovered. Diagnosis: clinical septicemia, five cases; positive blood cultures, seventeen; streptococcus, nine; staphylococcus, six; pneumococcus, three; diplococcus, one and *Bacillus coli*, one.

Dosage of mercurochrome-220, intravenous: nine received one injection, in every case, 5 mg. per kilogram or more. One patient received 7.5 mg. per kilogram, another 8 mg. per kilogram twice, and three five or more injections of from 4 to 5 mg. per kilogram. No patient developed nephritis.

TABLE 5.—*Summary of Cases of Septicemia in Group I*

Group	Classification by Origin	Total No.	Cure Probably Due to Mercurochrome-220	Great Improvement after Mercurochrome-220	Improvement but Later Complications	Action of Mercurochrome-220 Doubtful	Failed
A	Urinary	1	1	..	..	..	1
B	Traumatic or postoperative	12	5	4	1	..	2
C	Throat infection	6	5	..	..	..	1
D	Ear or lateral sinuses	2	1	..	..	..	1
E	Osteomyelitis or abscess	6	2	1	..	..	3
F	Puerperal	20	11	3	1	1	4
G	Endocarditis	7	2	..	..	..	5
H	Focus not found	2	1	..	..	..	1
		57	28	8	2	1	18

TWENTY-TWO CASES OF PNEUMONIA[67]

CASE 58 (Martyn[68]).—*Dental abscess. Pneumonia. Septicemia. Streptococcus hemolyticus. Intravenous injection of 5 mg. per kilogram of mercurochrome-220. Recovery.*

A woman had rapid pneumonia beginning with the left lower lobe, and swollen, painful joints, following a dental extraction. For several days the condition remained the same; then the right lower and middle lobes became infected. The temperature ranged from 102 to 104 and was typically septic. Cultures gave the *Streptococcus hemolyticus,* no pneumococci.

Tuesday, March 4, Dr. Martyn said that he was in despair. The patient was rapidly going down. The temperature was 104, the pulse 140. She was cyanotic; every joint was swollen. Dr. Martyn happened to open *The Journal of the American Medical Association* which had just come, and read an article by us. He immediately had the solution made up and gave 20 c.c. intravenously, allowing 5 mg. of 1 per cent. mercurochrome-220 per kilogram of weight. Within an hour, she began to experience rigor. This continued severely for three hours, the temperature going up to 105. Profuse perspiration followed, then sleep, and the next morning the temperature was 99.6, the pulse 96. She began to expectorate freely, the tongue cleaning. There were eight bowel actions in the first twelve hours. The appetite came back rapidly.

The most gratifying result of all was the cessation of all joint symptoms immediately. The temperature remained below 100, and today is normal. Dr. Martyn felt that the mercurochrome-220 had saved the patient's life.

This case is interesting as the first published report of the use of mercurochrome-220 in the cure of pneumonia.[69]

CASE 59 (Courtright[70]).—*Pneumonia of influenzal type. Desperately ill. Intravenous injection of 4.5 grains (0.29 gm.) of mercurochrome-220 in 1 ounce (30 c.c.) of water. Recovery.*

May 24, 1924, Dr. Courtright was called in consultation with Dr. Hatfield of Kingston, Ohio, in a case of a woman with pneumonia of the "1917 type of influenza." The patient was dreadfully sick, and Dr. Courtright thought that

67. Also Cases 21, 29 and 185.

68. Personal communication from Dr. George Martyn, Suite 906 Pacific Mutual Building, Los Angeles.

69. Young and Birkhaug (Footnote 19, eighth reference).

70. Personal communication from Dr. D. V. Courtright, Circleville, Ohio.

something had to be done and, as he said, done quickly. He gave an intravenous injection of mercurochrome-220, 4.5 grains (0.29 gm.) in 1 ounce (30 c.c.) of water. An hour later, the patient had a severe chill and the temperature rose to 105, after which it gradually subsided. In a short time purging began, the bowels moving almost continuously and all stools being dyed a deep red. The next morning the temperature was 99, and in the evening 101. On the following day, the temperature was almost normal and the condition much improved. After that there was continued improvement each day. Six days after the injection the patient was entirely well. The woman had been almost moribund, and Dr. Courtright considered the use of mercurochrome-220 intravenously a marvelous success.

CASE 60 (Case[68]).—*Bronchopneumonia. Two intravenous injections of mercurochrome-220 (5.3 mg. and 3 mg. per kilogram). Recovery.*

A girl, aged 2½ years, weighing 36 pounds (16.3 kg.) was first seen on the afternoon of Sept. 28, 1924, acutely ill with a temperature of 106. She was prostrated and had all the clinical signs of extensive bronchial pneumonia. She was sent to the hospital, and by tepid baths and colonic irrigations the temperature was reduced to 103. The patient, however, remained in a stupor. The pulse was 150, respiration 41. At 10 o'clock the same night, the patient being unimproved and still desperately ill, she was given 8.7 c.c. of 1 per cent. mercurochrome-220 (5.3 mg. per kilogram) intravenously. October 1, a second injection of 5 c.c. of 1 per cent. mercurochrome-220 (3 mg. per kilogram) was given. After this the patient began to improve rapidly. By the fifth day, she was greatly improved, and she was discharged from the hospital on the tenth day. After the eleventh day, there was never any cough, and a week later, the patient was entirely well.

A very important article on the use of mercurochrome-220 in the treatment of pneumonia has been presented by Freeman and Hoppe[15] from which we make the following extracts.

We had the opportunity of treating a series of cases of bronchopneumonia following an epidemic of measles at the Atlanta Child's Home. One child, desperately ill with extensive bronchopneumonia, multiple abscesses and severe diarrhea, was beginning the fifth week of illness. The results obtained by using mercurochrome-220 in this case led us to try it in others, and also to attempt to find some explanation of the mode of action. It was obvious that the drug might rid the blood of any bacteriemia by direct action. This, however, did not explain the results where no bacteria existed in the blood stream. We have, therefore, advanced the theory that the drug might leave the blood by a process of osmosis and incorporate itself in the lymph and tissue fluids, thereby coming in close contact with the areas of consolidation and the invading organisms. Some such explanation is necessary to explain the marked clinical improvement following the intravenous use of mercurochrome.

CASE 61 (Freeman and Hoppe,[15] Case 1).—*Bronchopneumonia. Intravenous injection of mercurochrome-220, 5 mg. per kilogram. Rapid recovery.*

M. L., a girl, aged 5½ years, white, weighing 12 kg., developed measles, Jan. 29, 1924. This was followed by bronchopneumonia and acute otitis media. She had been ill about six weeks, during which time her temperature had varied from 102 to 105. During the fourth week of illness, she developed severe diarrhea, having from five to seven foul stools daily. On the thirty-eighth day of her illness she was in a desperate condition. There were five separate areas of consolidation in the lungs; the temperature was 104.6; she was markedly

emaciated; both ears were discharging profusely, and she had numerous skin abscesses. The respiration was labored and the patient would become so cyanotic at times that hypodermic injections of epinephrin were required. Hope for her recovery having been abandoned, the physicians decided to try mercurochrome-220 soluble. She was given 0.005 gm. per kilogram of body weight intravenously. There was little or no systemic reaction. The temperature fell as if by crisis and she began a rapid and uninterrupted recovery. The stools were stained red for two days, but the diarrhea rapidly disappeared. The skin lesions improved. Drs. Freeman and Hoppe said that they never had seen a more spectacular recovery (Fig. 10).

Case 62 (Freeman and Hoppe,[13] Case 2).—*Bronchopneumonia following measles. Intravenous injection of mercurochrome-220, 5 mg. per kilogram. Rapid recovery.*

L. M. W., a girl, aged 6½ years, white, weighing 14 kg., was first seen March 4. She had developed measles one week before and, March 7, the

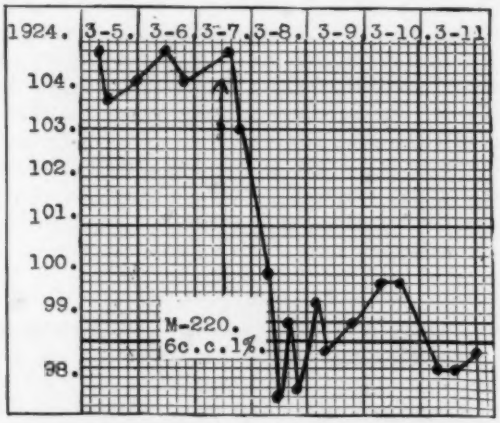

Fig. 10 (Case 61).—Temperature before and after intravenous injection of 6 c.c. of 1 per cent. solution of mercurochrome-220 soluble in case of bronchopneumonia.

temperature rose to 104, respiration became rapid and labored and cyanosis appeared. The patient was found to have areas of diminished resonance, crepitant râles and bronchial breathing in the right middle and lower lobes. On the fourth day of her illness, she received 0.005 gm. of mercurochrome per kilogram of body weight intravenously. The temperature fell from 104 to 99, and the patient appeared greatly improved. The following afternoon the temperature rose again to 104, and it was found that both ear drums were inflamed. They were incised, and the temperature dropped to normal. Three days later, the lungs had almost completely cleared. Recovery was rapid and complete.

Case 63 (Freeman and Hoppe,[13] Case 3).—*Bronchopneumonia following measles. Intravenous injection of three doses of mercurochrome-220, 5 mg. per kilogram. Rapid recovery.*

R. M., a girl, aged 11 months, white, who weighed 6.5 kg., March 9, developed bronchopneumonia following measles. There were scattered areas

of consolidation in both lungs, especially in the right lower lobe. The temperature varied between 100 and 104. She received 0.0046 gm. of mercurochrome per kilogram of body weight on the second day of her illness, and on the following day 0.006 gm. After this injection, the patient was greatly improved and the temperature fell to 100. It rose again on the following afternoon, and it was found that she had double otitis media. The drums were incised with gratifying results, but on the eighth day the temperature rose to 102.2 and further signs of pneumonia were found. She was again given 0.006 gm. of mercurochrome per kilogram of body weight, which was followed by a rapid fall in temperature. The lungs quickly cleared. Recovery was complete.

CASE 64 (Freeman and Hoppe,[15] Case 4).—*Lobar pneumonia. Two intravenous injections of mercurochrome-220, 4.6 mg. and 6 mg. per kilogram. Rapid recovery.*

M. D., a girl, aged 1 year, colored, who weighed 6½ kg., was markedly emaciated. She was admitted to the Brady Hospital on the second day of illness, with lobar pneumonia involving the right upper lobe and a severe ulcerative stomatitis. On the fourth day of illness the child was extremely ill and almost comatose. She received 0.0046 gm. of mercurochrome-220 per kilogram of body weight. The temperature fell to 100 on the following day and the patient was much brighter, but still showed signs of pneumonia. Accordingly she was then given 0.006 gm. of mercurochrome per kilogram of body weight. This was followed by a slight rise in temperature and several red stools. The patient was greatly improved after this injection. The pneumonia resolved rapidly. The stomatitis was apparently not affected.

CASE 65 (Freeman and Hoppe,[15] Case 5).—*Bronchopneumonia following measles. Mercurochrome-220, 5 mg. per kilogram. Rapid recovery.*

M. J., a boy, aged 9 months, white, who weighed 8 kg., developed measles complicated by bronchopneumonia. When the patient was seen on the eighth day of illness, there was a small area of consolidation in the left lower lobe and many moist and crepitant râles throughout both lungs. Respiration was rapid and of a grunting character, and cyanosis was marked. He received 0.005 gm. of mercurochrome per kilogram of body weight intravenously. The following day, although there was no marked change in temperature, clinically he was greatly improved. The respiration was much slower and cyanosis had disappeared. Recovery was uneventful.

CASE 66 (Freeman and Hoppe,[15] Case 6).—*Three intravenous injections of mercurochrome-220, 5 mg. per kilogram. Death on seventeenth day.*

W. M., a boy, aged 5 years, white, who weighed 16 kg., had been in the Atlanta Child's Home for several years, and had always been slightly cyanotic without any known cause. He developed measles followed by bronchopneumonia. On the eighth day of illness, he received 0.005 gm. of mercurochrome per kilogram of body weight. The temperature fell and clinically he was much improved. On the twelfth day, otitis media developed, which required incision of the drums. The following day the patient was worse and the original dose of mercurochrome was repeated. He continued to be very cyanotic, although the temperature was never high. On the fourteenth day, he received a third injection of mercurochrome. The physical signs were still those of bronchopneumonia, though not so extensive as at first. The temperature was only 100. However, he continued to grow weaker and it was decided to admit him to the Brady Hospital, where he died three days later. Permission

to perform a complete necropsy was not obtained. The lungs were examined and extensive congestion was found. The immediate cause of death was undetermined.

CASE 67 (Freeman and Hoppe,[18] Case 7).—*Lobar pneumonia. Intravenous injection of mercurochrome-220, 5 mg. per kilogram. Rapid recovery.*

C. C., a boy, aged 6 years, colored, who weighed 19 kg., was admitted to the Grady Hospital with lobar pneumonia involving almost the entire right upper lobe. The temperature varied from 100 to 105.5. On the eighth day of illness, the patient received 0.005 gm. of mercurochrome per kilogram of body weight. This was followed by a slight rise in temperature and a very rapid fall to normal. The change in his general condition following the use of mercurochrome was remarkable. Complete recovery followed rapidly.

CASE 68 (Freeman and Hoppe,[18] Case 8).—*Lobar pneumonia. Intravenous injection of mercurochrome-220, 5 mg. per kilogram. Recovery.*

J. B., a boy, aged 3 years, colored, who weighed 12 kg., entered the Grady Hospital with lobar pneumonia involving the right lower lobe. The temperature varied from 100 to 104.4. On the fourth day of illness the patient received

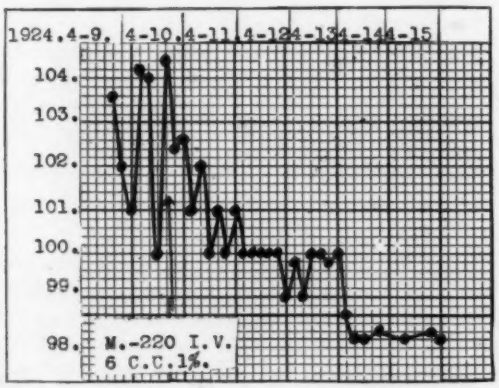

Fig. 11 (Case 68).—Temperature before and after intravenous injection of 6 c.c. of 1 per cent. solution of mercurochrome-220 soluble in case of lobar pneumonia.

0.005 gm. of mercurochrome per kilogram of body weight. The fall in temperature was rapid, and although it remained at 100 for a few days, the breathing was comfortable, the child had lost his anxious expression, and he showed marked clinical improvement. Recovery was rapid and complete.

CASE 69 (Freeman and Hoppe,[18] Case 9).—*Lobar pneumonia. Two intravenous injections of mercurochrome-220, 5 and 4.6 mg. per kilogram. Recovery.*

R. B., a boy, aged 8 years, colored, who weighed 24 kg., was treated in the Grady Hospital for lobar pneumonia. On admisison, there was complete consolidation of the right lower lobe. On the sixth day of illness, he was given 0.005 gm. of mercurochrome per kilogram of body weight intravenously. Before the injection, he was very restless. The respiration was 72 a minute and grunting in type, and the child gave every evidence of being very ill. The following morning there was only a slight change in temperature, but the boy was found sitting up in bed eating an orange. That afternoon he appeared worse and it was then that beginning involvement of the left lower lobe was

discovered. He was given 0.0046 gm. of mercurochrome per kilogram of body weight. After a brief rise in temperature, which fell rapidly to normal, the patient was greatly improved and the lungs promptly cleared.

CASE 70 (Freeman and Hoppe,[15] Case 10).—*Bronchopneumonia; "almost moribund." Intravenous injection of mercurochrome-220, 1.5 mg. per kilogram. Death.*

C. C., a boy, aged 5 years, colored, who weighed 19 kg., was admitted to the Brady Hospital with severe bronchopneumonia. On admission the patient was almost moribund. There were several areas of consolidation and many moist and crepitant râles throughout both lungs. The condition became rapidly worse and though it was quite apparent that he was dying, he was given 0.0015 gm. of mercurochrome per kilogram of body weight. (This we consider too small a dose). The dose was without effect, and the patient died one hour later.

CASE 71 (Freeman and Hoppe,[15] Case 11).—*Lobar pneumonia. Two intravenous injections of mercurochrome-220, 5 and 4.6 mg. per kilogram. Recovery.*

T. J. H., a boy, aged 8 years, colored, who weighed 24 kg., was admitted to the Grady Hospital on the fourth day of illness, with lobar pneumonia involving the right lower lobe. The following day the patient received 0.005 gm. of mercurochrome per kilogram of body weight. The temperature fell 3 degrees and the child was much improved. He was given 0.0046 gm. the next day, with marked benefit. The temperature promptly fell to normal, convalescence was uneventful and recovery complete.

CASE 72 (Freeman and Hoppe,[15] Case 12).—*Bronchopneumonia following measles. Intravenous injection of mercurochrome-220, 4.6 mg. per kilogram. Recovery.*

B. M., a girl, aged 8 months, white, who weighed 7.5 kg., developed bronchopneumonia following measles. The temperature varied between 103 and 105; the respiratory rate was 60, and cyanosis was marked. There was a definite area of consolidation in the right lower lobe, and many moist and crepitant râles throughout both lungs. On the third day of illness, the patient received 0.0046 gm. of mercurochrome per kilogram of body weight intravenously. The sudden drop in temperature and the rapid recovery following the use of mercurochrome in this case was spectacular.

Freeman and Hoppe drew the following summary of the twelve cases quoted:

Of the twelve cases of pneumonia, seven were bronchopneumonia and five were lobar in type. Two patients died. In one, death was inevitable before the drug was given. The other case, with cyanosis of unknown origin existing for several years, showed definite improvement at first but later failed to respond to treatment.

In seven cases one injection was all that was required. Three cases required two injections and three injections were given in two cases. The average dose was 0.005 gm. per kilogram of body weight, using a 1 per cent. solution.

We should like to call attention to the fact that a very marked clinical improvement usually occurs a few hours after the injection, and that this improvement sometimes occurs without any marked change in the temperature or pulse rate.

It was our observation that these cases of pneumonia treated with mercurochrome ran a much shorter course than cases of pneumonia of the same severity in which this drug was not used.

The recent paper of Hoppe and Freeman before the Southern Medical Association is a splendid exposition of their results in pneumonia in children. Their work is so important that we quote as follows:

Our observations on the effect of this drug on pneumonia are based on a series of forty-six cases, of which twenty-three were bronchopneumonia and twenty-three lobar in type. Of these forty-six cases, twenty-three received mercurochrome and twenty-three were used as controls. These were all observed in one institution during the same season of the year and were, therefore, probably infected by the same types of organisms. Except for the fact that one-half the group received mercurochrome, the treatment was the same in each case. As near as we could determine, the severity of the disease was about equal in the two groups. If there was any difference the more severe ones were treated with mercurochrome.

Of the twenty-three control cases, the average duration of illness was sixteen and one-half days, while with those receiving mercurochrome the average duration of illness was six and one-half days. With three of these the crisis occurred on or before the third day. The twenty-three cases treated with mercurochrome were sick on an average of two and one-fourth days after the first dose was given. The mortality of the control group was 39 per cent. Of those treated with mercurochrome the mortality was 8.5 per cent.

The clinical results obtained by the use of this drug are probably due, first, to the bactericidal action of mercurochrome on any bacteria in the blood stream and, second, to inhibition of the growth of bacteria in the lungs.

We have been greatly interested in the reports of the use of mercurochrome in other conditions and have read with no little surprise the accounts of frequent untoward reactions, especially in adults. We are at a loss to account for these, as none of our cases have shown the slightest serious reactions.

Three additional cases of Hoppe and Freeman, from this paper, follow.

CASE 73 (Freeman and Hoppe, Case 13).—*Lobar pneumonia. Intravenous injection of mercurochrome-220, 5 mg. per kilogram. Rapid recovery.*

R. L., a boy, aged 3 years, 10 months, developed lobar pneumonia, May 17, 1924. When seen on the second day of his illness there was a complete consolidation of the left upper lobe. The following evening he was in a desperate condition. The temperature was 104.4, respiration 60, and the patient markedly cyanotic. An intravenous injection of mercurochrome-220, 5 mg. per kilogram, was made. The temperature was normal in eight hours; cyanosis had completely disappeared, and the respiratory rate was about normal. Recovery was rapid and complete.

CASE 74 (Freeman and Hoppe, Case 19).—*Lobar pneumonia. Mercurochrome-220, 5 mg. per kilogram intravenously and 5 mg. per kilogram intraperitoneally. Rapid recovery.*

F. H., a girl, aged 10 months, was brought to the office the day before the onset of her illness for advice as to diet regulation. At that time, the temperature was normal and the lungs were clear. The next morning the temperature was 100. Dulness and diminished intensity of the breath sounds were discovered in the left upper lobe. The following morning, the temperature was 105.2 and there were marked dulness, bronchial breathing and many crepitant râles in the area just described. She was given an intravenous injection of mercurochrome-220, 5 mg. per kilogram. The following morning she

was much improved but still showed some evidence of pneumonia. She was given a second injection of mercurochrome-220. This time the intraperitoneal route was used. The temperature promptly fell to normal, and the lungs cleared rapidly. The total duration of the illness in this case was sixty-four hours.

CASE 75 (Freeman and Hoppe, Case 20).—*Bronchopneumonia. Two intraperitoneal injections of mercurochrome-220, 5 mg. per kilogram. Recovery.*

A colored infant was admitted to the Brady Hospital with a bronchopneumonia of twenty-four hours' duration. She was found to have a small area of consolidation in the right middle lobe and many moistened crepitant râles through both lungs. She was given 5 mg. per kilogram of mercurochrome-220 in the peritoneal cavity. The temperature promptly fell to normal and the patient became much improved. Two days later, breathing became rapid and the temperature rose to 100. She was given a second intraperitoneal injection of mercurochrome-220. This was followed by a slight rise in temperature, which promptly fell to normal. The lungs cleared rapidly.

CASE 76 (Davis[71]).—In this case of lung abscess, the patient was taken with a severe pain in the right side of the chest Oct. 16, 1924. October 20, the pain in the chest was continuous, the temperature being 103.6. Examination showed dulness on percussion over the right side of the chest. Roentgen-ray examination showed a circumscribed area (shadow) in the middle of the right side of the lung about two inches (5 cm.) in diameter. Diagnosis of a lung abscess was made.

October 21 and 22, the temperature reached 103.5. An intravenous injection of 21 c.c. of 1 per cent. mercurochrome-220 was given. The temperature fell to normal. The temperature never rose above normal after that, and on account of this there was doubt if it had been a beginning lung abscess or pneumonia, but even if it were a case of pneumonia, the cure was certainly immediate after injection. Roentgen-ray pictures taken before the patient went home, October 30, showed the lung perfectly normal.

CASE 77 (Bunten[22]).—A man, aged 21, entered the hospital in a critical condition suffering from bilateral lobar pneumonia. The temperature was 105 and he was delirious. He was treated several days without change, and as the fever remained high it was decided to give him an intravenous injection of mercurochrome-220, the first dose 10 c.c. of 2 per cent. solution. In forty-eight hours, this dose was repeated. There was a considerable reaction: marked salivation, loose teeth and gums bleeding and painful. These, however, cleared up in a week. The patient recovered from the pneumonia but developed an empyema on the right side which was drained. He left the hospital four weeks later feeling fine. The result from the use of mercurochrome-220 seemed very satisfactory.

CASE 78 (Roeder and Judd[21]).—A boy, aged 2½ years, presented a picture resembling pneumonia with possible infection in the region of the appendix. The cough, flushed face and marked coryza contraindicated abdominal operation. There was moderate rigidity of the abdominal muscles with considerable pain and tenderness throughout the abdomen and a general picture of extreme toxemia. Breathing was of the pneumonic type. The lungs presented numerous coarse moist râles through both bases. The temperature was 103, pulse 140, and respiration 50. Leukocytosis was 25,000. Forty-eight hours after admission, the abdominal picture became more marked, and under local anesthesia pus

71. Personal communication from Dr. C. R. Davis, Detroit, Mich.

was drained from the region of the appendix. Twenty-four hours following operation, the temperature was 105, pulse 160 and respiration 52. The patient looked as if recovery were impossible.

Eighteen cubic centimeters of 0.5 per cent. mercurochrome-220 was injected into the jugular vein, followed by a temperature of 107.5 and a pulse too fast to count. Five hours later the temperature was 102, pulse 120, and respiration 30. There was gradual recession of the temperature and pulse for several days. After this there was a rise of the temperature to 103, and the pulse to 140. Physical examination revealed typical lobar pneumonia of the right lower lobe. Four days later, the condition was again extremely critical. There was

TABLE 6.—*Results in Eighteen Cases of Pneumonia Treated by Mercurochrome-220 Soluble*

Case	Age	Diagnosis	Condition Stated	Intravenous Injection of Mercurochrome-220		Doctors' Comments
				No.	Mg. per Kg.	
58	?	Pneumonia; dental abscess; multiple arthritis	Condition desperate	1	5	Saved her life
59	..	Pneumonia after influenza	Almost moribund	1	5(approx.)	A marvelous success
60	2½	Bronchopneumonia	Patient in stupor	2	5, 3	Rapid recovery
61	5½	Bronchopneumonia; otitis media	Desperate condition	1	5	A spectacular recovery
62	6½	Bronchopneumonia after measles	Fair condition	1	5	Rapid recovery
63	11 mo.	Bronchopneumonia; otitis media; measles	Fair; temperature 104	2	6	Rapid fall in temperature
64	1	Lobar pneumonia; stomatitis	Almost comatose	2	4.6, 6	Rapid resolution
65	9 mo.	Bronchopneumonia following measles	Marked cyanosis	1	5	Recovery uneventful
66	5	Bronchopneumonia; otitis media; measles	Grew gradually weaker	3	5, 5, 5	Died
67	6	Lobar pneumonia	Temperature 105.5	1	5	Remarkable change; well
68	3	Lobar pneumonia	Temperature 104.4	1	5	Recovery rapid
69	8	Lobar pneumonia	Very ill	2	5, 4.6	Lungs promptly cleared
70	5	Bronchopneumonia	Moribund	1	1.5	Died one hour later
71	8	Lobar pneumonia	Right lower lobe involved	2	5, 4.6	Marked benefit; well
72	8 mo.	Bronchopneumonia following measles	Both lungs involved	1	4.6	Spectacular recovery
73	3	Lobar pneumonia	Desperate condition	1	5	Rapid recovery
74	10 mo.	Lobar pneumonia	Temperature 105.2; both lungs involved	2	5, 5	Total duration 64 hours; well
75	Infant	Bronchopneumonia	Both lungs involved	2	5, 5	Lungs cleared rapidly

almost continuous vomiting and toxemia. The temperature was 104, the pulse 150, and the patient was almost comatose. An intravenous injection of 18 c.c. of 0.5 per cent. mercurochrome-220 was given. Immediate and continuous improvement lasted for eight days. The temperature again subsided. A subdiaphragmatic abscess developed and was evacuated through the wound. On the fifteenth day, a second injection of mercurochrome-220 was given. In twenty-four hours the patient appeared greatly improved and went on to a rapid and complete recovery.

CASE 79 (Hopkins[72]).—A girl, aged 4 years, admitted March 24, 1924, with acute empyema following pneumonia and bilateral otitis media, had a pulse

72. Personal communication from Dr. F. S. Hopkins, Springfield, Mass.

of 160. Immediate drainage of the empyema was done. Dakin's solution was used every three hours. The patient continued restless and irritable, and her condition was very poor.

March 31, an intravenous injection, 15 c.c., of 0.4 per cent. mercurochrome-220 was given without any reaction. For nearly a week following this, she seemed stronger. The temperature was 99.6. She then grew rapidly weaker and died, April 8. In this case, there was improvement after mercurochrome-220, but the child was unable to stand the continued infection.

We have grouped in Table 6 a series of cases of pneumonia which exemplify the effect of intravenous injections of mercurochrome in such cases.

In the eighteen cases given, there were two deaths, one patient being moribund before injection. Sixteen recovered, of whom four were in a "desperate condition," one being called "almost moribund" and one "almost comatose." In eight cases, only one injection was required, but in all 5 mg. per kilogram was used. In seven cases, two injections of 5 mg. per kilogram (approximately) were used, and in one 3 mg. Apparently in no case did nephritis follow. The rapidity of cure was said to be spectacular in several cases. In the twenty-two cases recorded, there were three failures: Case 70 was said to be "moribund," Case 79 received only one injection of 2 mg. per kilogram, but Case 66 died after three full doses, 5 mg. per kilogram.

It seems fair to deduce that with large and, if necessary, multiple doses (5 mg. per kilogram each) a large percentage of recoveries may be expected in certain pneumonias, particularly in children. The number of adult cases is still too small to warrant positive assertions. In children the results appear to be really brilliant.

TABLE 7.—*Results of Mercurochrome-220 Soluble in Twenty-Two Cases of Group II Pneumonia*

Total	Infection Aborted or Recovery Probably Due to Mercurochrome-220	Marked Improvement after Mercurochrome-220	Failure
22	13	6	3

GENITO-URINARY INFECTIONS (NONGONORRHEAL)

FOUR CASES OF RETROPERITONEAL AND PERINEPHRITIC INFECTIONS

In the two cases here cited, mercurochrome-220 has proved very effective in combating retroperitoneal and perinephritic infections. Case 80 is the first published demonstration of the positive value of mercurochrome-220 as an intravenous germicide in local and general infections.[73]

73. Young, H. H.: The Cure of a Retroperitoneal Infection (Abscess) by the Intravenous Injection of Mercurochrome-220, Bull. Johns Hopkins Hosp. **35**:14 (Jan.) 1924.

CASE 80 (Young and Hill[27]).—*Retroperitoneal abscess following bladder instrumentation. Colon bacillus infection. Intravenous injection of 5 mg. per kilogram of mercurochrome-220. Rapid disappearance of abscess.*

J. H. D., a youth, aged 17, admitted June 21, 1923, had a hypospadias, for which a plastic operation was done to close the defect. The convalescence was uneventful until July 14, the twenty-third day, when, following the passage of sounds, the patient had a chill and fever which reached 101.5. On the following day, the patient was very ill, and the temperature reached 104. He complained of pain in the left side, extending up the small of the back, and on examination there was muscle spasm and tenderness on pressure. A diagnosis of retroperitoneal infection following instrumental laceration of the urethra or bladder was made. On the next day, the muscle spasm and mass had increased and a definite diagnosis of retroperitoneal abscess was made. The patient's temperature at 8 o'clock was 103.5. Examination of the urine showed an infection of colon bacilli.

Ordinarily the patient would have been taken to the operating room for immediate incision and drainage of the abscess, but we decided to try mercurochrome-220 intravenously, and 27 c.c. of 1 per cent. solution (5.4 mg. per kilogram) was given at 11 a. m. At noon, the temperature was 106, and the patient had a severe chill, but by midnight it had dropped to 99.6 and after that remained practically normal. On the following day, the patient was free from pain; the muscle spasm had largely disappeared, and he went on to a rapid recovery without operation. December 15 (final report), the patient was quite well. June 15, 1924, an examination of the urine was sterile.

The foregoing detailed case is of interest as being the first recorded case in which a localized infection was cured by intravenous injection of mercurochrome-220, and in fact the first published report of the successful use of mercurochrome-220 as an intravenous germicide.

CASE 81.—*Perinephritic abscess (staphylococcus infection). Intravenous injection of 5 mg. per kilogram of mercurochrome-220, and gentian violet, 5 mg. per kilogram. Recovery.*

W. M. A., a man, aged 22, was admitted to Brady Urological Institute, July 24, 1924, complaining of a dull pain of eight days' duration over the left renal region. On admission, the temperature was 101.6 and the white blood cells totaled 17,240. Examination revealed a mass from 3 to 4 inches (7.6 to 10.1 cm.) in diameter between the middle of the crest of the ilium and the costal margin. This mass, which extended backward beneath the lumbar muscle, was very tender on deep pressure. On the following day, the white blood cell count was 20,000. A double ureteral catheterization showed that neither kidney was infected. The mass was aspirated, pus cells and staphylococci being obtained on culture. A diagnosis of perirenal abscess was made and an intravenous injection of mercurochrome-220 (5 mg. per kilogram) was given. This was followed by a severe chill, nausea and vomiting, and the temperature rose to 103.6, but by noon the next day it was again normal. It remained normal until the patient's discharge five days later. The pain had entirely disappeared within twenty-four hours, and at the time of his discharge the mass was not palpable and the white blood cells had dropped to 8,700.

He returned five days later with pain. There was slight muscle spasm and considerable tenderness over the left flank, but no mass was felt. The temperature ranged from 99 to 100 and the white blood cells totaled 17,240. An examination of the urine showed a staphylococcus infection. He was given

an intravenous injection of mercurochrome-220, 5 mg. per kilogram, following which the temperature became normal and the pain decreased in intensity. However, on the next day his condition was about the same as on admission, so he was given 5 mg. per kilogram of gentian violet. Aside from a decided drop in the white blood cells, to 10,120, no change was observed. In view of the persistent staphylococcus infection of the urine, he was given hexylresorcinol, 10 grains (0.65 gm.) three times a day by mouth. The condition gradually improved, the urine becoming sterile, and when discharged two weeks later he was asymptomatic and apparently well.

CASE 82 (Slaughter[74]).—In this case of perinephritic abscess, the temperature was 103. An intravenous injection of 3.5 mg. per kilogram of mercurochrome-220 was given. In two days, mass, tenderness and elevation of temperature were gone. The patient was cured.

CASE 83 (Slaughter[74]).—In this case of perinephritic infection, there was severe pain. An intravenous injection of mercurochrome-220, 3.1 mg. per kilogram, was given, and a second dose of 2.3 mg. per kilogram. The fever and pain disappeared. The patient was much improved.

TWENTY-THREE CASES OF PYELONEPHRITIS[75]

The first successful record[26] of mercurochrome-220 in pyelonephritis is given in Case 84. This, in fact, is the first case in which we succeeded in proving that mercurochrome-220 injected intravenously in the human subject would sterilize an infection, although we had previously succeeded in animals. Piper had also tried it but declared, in the report[11] of his cases, "these cases are certainly not definitely conclusive that in mercurochrome-220 soluble we have found a cure for blood stream infection."

Five cases of pyelonephritis are given below in detail. In all the cases the urine was sterilized by mercurochrome-220 given intravenously, assisted by gentian violet and neo-arsphenamin in two cases.

CASE 84 (Young and Hill[27]).—*Bilateral chronic pyelonephritis due to Bacillus lactis-aerogenes. Intravenous injection of 5 mg. per kilogram of mercurochrome-220. Sterilization.*

A woman, admitted to Brady Institute, Jan. 2, 1923, complained of pain in the left side of six months' duration, and of frequency of urination. Ureteral catheterization showed pus and bacilli from the right kidney. During the following week, the patient was treated by pelvic lavage three times. Cultures were obtained from the right kidney, and were found to be *Bacillus lactis-aerogenes.* Cultures from the left kidney were at first sterile, but later showed bacilli. As the pelvic lavage was unsuccessful in clearing up the renal infection (both 1 per cent. meroxyl and 1 per cent. silver nitrate solution had been used), January 12, she was given an intravenous injection of 1 per cent. of mercurochrome-220, 5 mg. per kilogram. Marked nausea followed, and half an hour later vomiting and a large stool. In six hours, the patient was comfortable. The temperature remained normal. On the following day, the urine was found to

74. Personal communication from Dr. J. H. Slaughter, Bogalusa, La.
75. Reference should also be made to Case 1.

contain numerous bacilli (probably dead), but the cultures were sterile. Casts were present for a few days. On discharge from the hospital, January 26, the urine was sterile; there was a trace of albumin and an occasional cast. The pain and discomfort had completely disappeared. Subsequent cultural examination showed the urine to be sterile, no bacilli present, no albumin and no casts.

This case is interesting as being the first recorded case of the cure of renal infection by mercurochrome-220 given intravenously. It was also the first case of the successful use of mercurochrome-220 intravenously.

CASE 85 (Young and Hill [77]).—*Pyelonephritis, acute. Mercurochrome-220 and gentian violet, intravenously. Recovery.*

R. M., aged 63, was admitted to Brady Institute, June 28, 1923, with tumor of the bladder. July 9, a resection was done. September 5, there were chill, fever and pain with a tender mass in the region of the left kidney. The patient continued to have daily pyrexia and rapidly grew worse, until it seemed evident that a fatal ending would soon ensue. The mass in the left kidney was considerable. An operation was contraindicated by the desperate condition of the patient. September 23, an intravenous injection of mercurochrome-220, 5 mg. per kilogram, was given. Within three hours, bacilli previously present in the urine had disappeared completely and the gram-positive cocci were greatly reduced in number. The temperature fell to normal and remained so for two weeks. The patient greatly improved. As the urine still contained large numbers of staphylococci and streptococci, he was then given 0.6 gm. of neoarsphenamin intravenously. The result was slight benefit. October 11, an intravenous injection of 28 c.c. of 1 per cent. mercurochrome-220, 5 mg. per kilogram, was given. There was no reaction. The fever disappeared, and the patient continued to improve. The pain and tenderness in the region of the left kidney disappeared. The urine still contained a few staphylococci. Convalescence was satisfactory. The patient was discharged, apparently well. December 5, the patient wrote that he was "entirely well."

CASE 86 (Stirling [76]).—*Pyelonephritis. Staphylococcus. Mercurochrome-220, 3 mg. per kilogram. Urine sterilized. Recovery.*

A woman, aged 45, was admitted in April, 1924, complaining of pain in the back and right side, and suprapubic pain, frequency of urination, dysuria and a history of frequent pyrexia.

A ureter catheterization showed pus in large quantities on the right side, with staphylococci on the slide and in the cultures. The urine from the left side showed pus in a small amount and an occasional staphylococcus on the slide and in the culture. A pyelogram was not done. A general phenolsulphonephthalein test showed practically normal kidney function.

The patient was treated by renal lavage on both sides with 1 per cent. silver nitrate, two treatments being given without marked improvement. The patient was then given mercurochrome-220 (about 3 mg. per kilogram) followed by practically no reaction. The temperature became normal, but the leukocytes, which had previously been 15,000, dropped to 10,000. In about four days, the temperature rose and the patient was given a second injection of the same dosage. There was no reaction and the injection was almost immediately followed by marked improvement in every respect. The urine became sterile

76. Personal communication from Dr. W. E. Stirling, Washington, D. C.

after the second injection. It was then clear, free from pus and bacteria on stained specimens. The patient was discharged as cured. She has reported since that time that she has remained well.

CASE 87 (Stirling[76]).—*Pyelonephritis. Staphylococcus aureus. Intravenous injection of mercurochrome-220, 4 mg. per kilogram once, and 5 mg. per kilogram twice. Urine sterilized. Recovery.*

A man, aged 45, was admitted about May 1, 1924, complaining of pain, frequency of urination and chills and sweats.

Examination showed tenderness in the region of both kidneys and in the costovertebral angle. Cystoscopy and a pyelogram were done. A diagnosis was made of pyelonephritis with contracted pelves (right 1 c.c.; left 2 c.c.). The phenolsulphonephthalein test showed 40 per cent. for two hours (30 per cent. the first hour, 10 per cent. the second hour). The kidneys were about equal in value. A ureter catheterization showed pus from each side (considerable amount). The red blood cells were considerable. The urine showed an infection with *Staphylococus aureus* on slides and in the cultures.

The patient was treated three times by lavage of the kidney pelves with 1 per cent. silver nitrate with marked improvement. The chills subsided; the urine became clear, and the pain was less intense. Two months later, he returned with a history of recurrent chills, pain and dysuria. The patient refused cystoscopic treatment on account of his previous experience with pain. It was then decided to give him 20 c.c. of a 1 per cent. solution of mercurochrome-220 intravenously, the dosage being about 4 mg. per kilogram. The temperature rosé to 104, and the patient had a severe chill. In about an hour, the patient felt better.

Two days later he was greatly improved, but as the urine still contained pus and staphylococci another treatment was given (30 c.c. of 1 per cent. solution). This was about 5 mg. per kilogram. The reaction which lasted for thirty minutes was less pronounced; the temperature rose to 101. Following this the dysuria largely disappeared, and the patient was much more comfortable and free from pain. The temperature remained normal, but the urine contained cocci. Therefore, after four days, the patient was given the third injection of mercurochrome (5 mg. per kilogram intravenously). The reaction was slight. The temperature was 100. At no time after any injection did the patient have nausea, vomiting or diarrhea. The urine and sputum were fairly deeply stained with mercurochrome-220. A day or two later, examination showed the urine to be clear from pus and no bacteria present on the slides or in the cultures. The patient has not reappeared, and the physician thinks that this in an indication that he has been cured.

CASE 88 (Young and Hill[77]).—*Pyelitis due to colon bacillus. A child, very septic. Four intravenous injections of mercurochrome-220, 8 and 2.5 mg. per kilogram. Child's life saved but urine not sterilized.*

M. L., a girl, aged 4 years, weighing 26 pounds (11 kg.) was admitted to the Harriet Lane Home, Nov. 2, 1923, complaining of pain in the right side of two days' duration. The patient was very sick; the temperature was 102.5, and the abdomen was rigid, with marked tenderness over both kidney regions. The urine was cloudy and contained pus and *Bacillus coli.* During the first two days, the temperature reached 105. On the third day, the patient was very ill, and it was decided to administer an intravenous injection of mercurochrome-220. Accordingly, 100 mg. was given, 8 mg. per kilogram. Following the injection, the temperature fell to 98. The next day the patient was much better, but she

continued to have a fever. During the next five days, she received four intravenous injections of mercurochrome-220 of 30 mg. each., 2.5 mg. per kilogram. Under this treatment, the temperature finally reached normal on the eighth day (Fig. 12). She then developed a furuncle. The temperature rose to 102.5. Bacteria were still present in the urine on discharge of the patient.

Case 89 (Redfern[77]).—In this case of pyelitis, an intravenous injection of 5 mg. per kilogram of mercurochrome-220 was made. The temperature was 103; it fell to normal and remained so.

Case 90 (Stirling[78]).—In a case of bilateral pyelonephritis, two intravenous injections of mercurochrome-220 were given. The urine became free from pus. The patient was cured.

Case 91 (Slaughter[74]).—A patient had pyelitis, cystitis, furunculosis and arthritis of the hips, knees and wrists. An intravenous injection of mercurochrome-220 was given. The urine cultures were sterile. Dr. Slaughter said

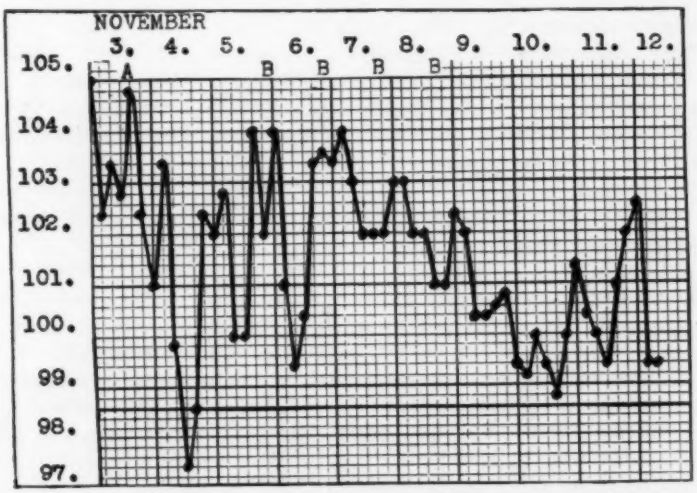

Fig. 12 (Case 88).—Temperature of child, aged 4 years, with pyelitis, due to colon bacillus, and sepsis, who showed marked improvement after five intravenous injections of mercurochrome-220 soluble. *A*, 8 mg. per kilogram injection; *B*, 2.5 mg. per kilogram injection.

that one would have to have seen the suffering of the patient to appreciate the wonderful result obtained by mercurochrome-220.

Case 92 (Slaughter[74]).—A patient with pyelocystitis was given two intravenous injections of mercurochrome-220 (dose not stated). The temperature became normal. Recovery followed.

Case 93 (Little[78]).—In a case of bilateral pyelonephritis cultures yielded staphylococcus and *Bacillus coli*. An intravenous injection of 4.2 mg. per kilogram mercurochrome-220 was given. There was pronounced improvement. The urine was sterile.

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77. Personal communication from Dr. T. C. Redfern, Winston-Salem, N. C.
78. Personal communication from Dr. J. E. Little, Fort Smith, Ark.

CASE 94 (Snitkay[79]).—A patient had pyelitis and cystitis. Cultures yielded streptococcus, staphylococcus and *B. coli*. The white blood cells totaled 28,000. An intravenous injection of 2.2 mg. per kilogram of mercurochrome-220 was given. Eight hours later, the temperature was 99.2. There was rapid recovery. The urine was sterile.

CASE 95 (Roeder and Judd[81]).—In a case of left pyelonephritis and hematuria, cultures yielded *B. coli*. An intravenous injection of 30 c.c. of 1 per cent. mercurochrome-220 was made, with complete disappearance of pain and hematuria. The patient was pronounced cured.

CASE 96 (Walston[80]).—In a case of pyelitis and cystitis, cultures yielded *B. coli*. Mercurochrome-220, intravenously, 3.8 mg. per kilogram; 3.8 mg. per kilogram; 1.5 mg. per kilogram was given. Recovery was rapid. The case was followed for seven months.

CASE 97 (Walston[80]).—A patient had pyonephrosis and cystitis and was seriously ill. Cultures yielded *B. coli*. The temperature was 105. Two intravenous injections of 24 c.c. of 1 per cent. mercurochrome-220 were given. Two days later the temperature was normal. There was no return of symptoms, although the case was followed for eight months.

CASE 98 (Slaughter[74]).—The patient had pyelitis. The white blood cells totaled 11,000. An intravenous injection of 20 c.c. of 1 per cent. mercurochrome-220, 3.1 mg. per kilogram, was given. The pain, which was severe, disappeared. The patient was discharged in good condition.

CASE 99 (Case[88]).—The patient had pyonephrosis. The temperature was 103.4. The patient was in a stupor. An intravenous injection of mercurochrome-220, 4.4 mg. per kilogram, was given. The temperature which was 103.4, fell in four hours to 99.5. Twelve days later, nephrectomy was done. The patient recovered.

CASE 100 (Little[73]).—The patient had double pyelitis. Cultures yielded *B. coli*. Two intravenous injections of 1 per cent. mercurochrome-220, 4.7 mg. per kilogram, were given. There was a slight reaction. The patient became much improved, and the condition cleared up under repeated pelvic lavages.

SIX CASES OF PYELONEPHRITIS IN WHICH PATIENT WAS UNIMPROVED

CASE 101 (Bruns[81]).—*Nephrolithiasis. Acute, suppurative, bilateral pyelitis. Staphylococcus aureus. Two intravenous injections of mercurochrome-220 without result. Four intravenous injections of neo-arsphenamin. Recovery. Sterilization of urine.*

A man, with left nephrolithiasis, following ureteral catheterization had a marked febrile reaction, pus and *Staphylococcus aureus* in the urine. There was pain over both kidneys. From this time, May 7 to July 29, 1924, the urine was always very purulent, *Staphylococcus aureus* being present. Hexamethylenamin in doses up to 80 grains (5.1 gm.) was given daily without result. Five injections of staphylococcus autogenous vaccine were given without result. Acriflavine pills, 1 grain (0.06), were given three times daily without result. July 12, an intravenous injection of 20 c.c. of 1 per cent. mercurochrome-220 was given. The temperature was 103. One week later,

79. Personal communication from Dr. C. J. Snitkay, Belle Plaine, Iowa.

80. Personal communication from Dr. E. B. Walston, Des Moines, Iowa.

81. Personal communication from Dr. E. H. Bruns, Chief of Medical Service, Fitzsimmons General Hospital, Denver. Mercurochrome-220 failed; the patient was cured by neo-arsphenamin.

15 c.c. of 1 per cent. mercurochrome-220 was given intravenously. There was a slight reaction. No improvement was noted in the urinary findings. July 27, 0.45 gm. of neo-arsphenamin was given intravenously. The urine at this time showed albumin, white blood cells and 60,800 colonies of *Staphylococcus aureus* per cubic centimeter of urine. The patient received four intravenous injections of neo-arsphenamin every other day, 0.45, 0.6, 0.75 and 0.9 gm. There were no untoward effects until the last dose. This was followed by repeated chills, high fever, profuse sweating, photophobia, muscle cramps and pains, stomatitis with foul breath and coated tongue, conjunctivitis, nausea and vomiting, a slight icteroid tint of the conjunctiva and slight tenderness over the liver. On the fourth day, a generalized maculopapular eruption appeared. The temperature then fell to normal, and the patient promptly recovered. Following the second injection of neo-arsphenamin, July 29, the urine became sterile and the number of pus cells decreased markedly. The urine remained sterile and by August 6 was perfectly normal. There has been no recurrence of symptoms since.

Case 103 (Little[78]).—The patient had pyelitis. Cultures yielded *B. coli* A blood culture was negative. An intravenous injection of 20 c.c. of mercurochrome-220, 5 mg. per kilogram, was given. A severe reaction followed. The infection persisted.

Case 103 (Little[78]).—The patient had pyelitis. Cultures yielded *B. coli* and staphylococcus. Three intravenous injections of mercurochrome-220, 4 mg. per kilogram, were given. There was pain and the staphylococci disappeared. Bacilli were still present in the urine.

Case 104 (Hinman[82]).—The patient had pyelitis and a ureteral stricture.

Case 108 (Hinman[82]).—The patient had prostatitis with obstruction, cystitis and pyelitis. A culture yielded *B. coli*. Two intravenous injections of 25 c.c. of 1 per cent. mercurochrome-220 were given. Vaccines and vigorous lavage were also used. Urine from the kidneys and bladder yielded *B. coli*; the heavy growth continued.

Case 106 (Piper[11]).—The patient had pyelitis. Two doses of mercurochrome-220 were given three days apart (amount not stated). The symptoms disappeared. There was still pus in the urine.

There were a number of cases treated in the Brady Institute in which the intravenous use of mercurochrome-220 failed to effect sterilization. They are given in detail in the chart on reactions. As previously stated, this list includes the following: A case of abscess of the seminal vesicle with *B. coli* and cocci present (the patient died and tuberculosis of the seminal vesicles was discovered), a case of bacilluria (*B. coli*); a case of periurethral abscess (*B. proteus* and streptococcus); a case of pansinusitis (pneumococcus, Type IV); two cases of endocarditis and septicemia (*Streptococcus viridans*); a case of peridental abscess; a case of chronic prostatitis (cocci); a case of pyonephrosis (staphylococcus);

82. Personal communication from Dr. Frank Hinman, San Francisco. Two intravenous injections of 30 c.c. of 1 per cent. mercurochrome-220 were given. Urinalysis showed pus and bacteria still present.

one case of generalized tuberculosis, diagnosed meningitis, and another case of generalized tuberculosis with severe urinary infection, and a case of pyelonephritis (*B. coli* and streptococcus).

In addition to these, there were several cases of colon bacillus pyelitis in which intravenous injection of mercurochrome-220 was entirely unsuccessful. In a very few of these cases it was successful, as shown elsewhere.

FOUR CASES OF CYSTITIS AND PROSTATITIS [83]

CASE 107 (Young and Hill [21]).—*Chronic cystitis. Staphylococcus and B. coli. Intravenous injection of mercurochrome-220, 3 mg. per kilogram. Cured.*

J. M. B., a man, aged 60, was readmitted, Oct. 13, 1923, complaining of frequency of urination. He had been subjected to a perineal prostatectomy one year previously, and a good result was obtained, with the exception of a vesical infection. Examination was negative except for cloudy urine, with pus and bacilli present in large numbers. The patient was treated by intravesical irrigations with benefit, but the urine was still heavily infected with colon bacilli and a small number of cocci.

October 12, he was given an intravenous injection of 20 c.c. (about 3 mg. per kilogram) of mercurochrome-220. He had no reaction, no rise in temperature, no vomitus and no stools. Within one hour, the urine showed colorimetrically a content of 1:20,000 mercurochrome-220. After the second hour, cultures and slide smears were negative, and remained negative for bacteria until the patient was discharged from the hospital, two days later. Cultures obtained ten days later showed that the urine was still sterile. April 30, a letter stated that the patient remained well.

CASE 108.—*Prostatitis and cystitis. Infection due to B. coli. Five intravenous injections of mercurochrome-220, from 3 to 4 mg. per kilogram. Urine and prostatic secretion sterilized.*

A man, aged 26, weighing 200 pounds (90.7 kg.) was admitted, Oct. 23, 1924, complaining of chills, fever and pus in the urine. Examination showed chronic prostatitis, cystitis, pus and *B. coli* in the urine. Five intravenous doses of mercurochrome-220, 3 mg. per kilogram, were given, four days apart, and two doses of 5 mg. per kilogram at two day intervals. Aside from slight nausea, the patient had no reaction. No red blood cells or casts appeared in the urine, and both urine and prostatic secretion were sterile on culture and slide smears after the sixth injection. The phenolsulphonephthalein test then showed 50 per cent. for two hours; before treatment was started, it had been 52 per cent. All symptoms of frequency, urgency and pain disappeared. November 25, the prostate was normal in size; the seminal vesicles were slightly indurated. The condition was greatly improved. The prostatic secretion showed a small amount of pus cells. No bacteria were present. The urine was negative. Repeated cultures were negative. The patient was discharged well.

CASE 109 (Slaughter [74]).—The patient had acute cystitis, with temperature of 104.8. Intravenous injections of 20 c.c. of mercurochrome-220 were given three times, followed by slight reaction. Two doses of 25 c.c. were given. All symptoms subsided; the urine was perfectly free from pus.

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83. Reference should also be made to Cases 116, 117, 118, 125, 129, 138, 139, 147, 148 and 150.

CASE 110 (Hopkins [72]).—A man, aged 39, weighing 170 pounds (77.1 kg.) had a urethral stricture. Urethrotomy was done and suprapubic cystotomy. There was a staphylococcus infection. Two doses of 30 c.c. of 1 per cent. mercurochrome-220 were given. There was little effect. The patient recovered.

CHRONIC CHANCROIDAL ULCERATION (EXQUISITELY PAINFUL)

The next case is a very remarkable demonstration of the effect of mercurochrome-220 on severe skin infections. The case was one of those chronic phagedenic chancroids which often go to progressive destruction of the entire penis.

CASE 111.—*Chronic chancroidal ulceration, extremely painful. Five intravenous injections of mercurochrome-220, 5 and 4 mg. per kilogram. Cured.*

R. F. B., a man, aged 28, admitted to Brady Urological Institute, Jan. 11, 1924, complained of sores on the penis of six months' duration. The ulcers had been treated in various clinics where roentgen ray, nitric acid, tartar emetic and numerous other forms of therapy had been tried and failed. Examination revealed an ulcer 1 cm. in diameter on the dorsal portion of the corona and a large, dirty, chronic ulcer about 3 mm. deep and 1 cm. broad which covered the whole left lateral side of the penis just in back of the corona. The ulcers were excruciatingly painful, and morphin was necessary. The temperature was moderately elevated, and the white blood count was 13,200. After all local antiseptics had failed and the Wassermann reaction was found to be negative, the ulcer on the dorsal portion of the corona was cauterized and the lateral ulcer completely excised by means of a cautery knife, and a circumcision was done. A pathologic study of the tissue removed showed chronic inflammatory tissue. Within a week, the entire wound had broken down and the same chronic process had again started, accompanied by great pain.

Cultures from the wound revealed gram-positive cocci, *Pseudomonas pyocyanea* and gram-negative bacilli. February 21, an intravenous injection of gentian violet, 5 mg. per kilogram, was given. No reaction followed, and no improvement in the ulcers or in the pain. The patient's condition was really desperate; he openly threatened suicide. It was decided to try mercurochrome-220. February 26, an intravenous injection of 5 mg. per kilogram was given. The temperature rose to 104. There were chill, nausea, vomiting, pain and no stools. Within two hours, the pain began to decrease in intensity and the next day for the first time the patient stated that he was free from pain. The serpiginous ulcer looked cleaner. February 28, an intravenous injection of mercurochrome-220, 5 mg. per kilogram, was given. No chill followed. The temperature was 100.8. There was stomatitis, but no nausea and no stools. The urine showed a faint trace of albumin and a few casts. From that time on his wound improved markedly, and healthy granulations started to form. March 12, an intravenous injection of mercurochrome-220, 4 mg. per kilogram, was given. No reaction followed. March 13, urinalysis was negative for albumin and casts. The wound was healing steadily. March 30, the patient was discharged. The condition was excellent. The wounds were healed; there was no pain. No morphin was taken. The urine was negative.

In the four cases of perinephritic abscess, the results were apparently uniformly good and in our two cases very striking, especially in Case 80,

in which a large inflammatory mass disappeared quickly. The total number of cases, however, is still too small for definite conclusions. In Cases 80 and 81, the dosage was 5 mg. per kilogram, in Case 82, 3.5 mg. per kilogram, and in Case 83, 3.1 and 2.3 mg. per kilogram.

Of the twenty-three cases of pyelonephritis, in seven cases the urine was sterilized and the patient relieved of all signs and symptoms. In two of these cases in which urine cultures yielded pure staphylococcus, Case 86 received 3 and 3 mg. per kilogram and Case 87, 4, 5 and 5 mg. per kilogram. In two cases of staphylococcus and other organisms, Case 93 with *B. coli* received 4.2 mg. per kilogram, and Case 94 with *B. coli* and streptococcus received only 2.2 mg. per kilogram.

In two cases with *B. coli* in pure culture, Case 95 received 5 mg. per kilogram and Case 96, 3.8, 3.8 and 1.5 mg. per kilogram.

Case 84, due to *B. lactis-aerogenes,* was sterilized by one dose of 5 mg. per kilogram.

In apparently none of the seven "cured" cases cited above was any other treatment used. In three cases, cultures and doses are not given but the patient is said to have been "cured" (Cases 90, 91 and 92). The patient improved greatly in seven cases: in Case 88 the child was desperately ill, the dosage was 8 mg. and four injections of 2.5 mg. per kilogram; "the patient's life was saved" but the urine still contained *B. coli.* Patient 85 was a man very ill with left pyonephrosis. Urine cultures yielded *B. coli,* streptococcus and staphylococcus. After intravenous injection of 5 mg. per kilogram of mercurochrome-220, the *B. coli* disappeared, and after intravenous injection of 5 mg. per kilogram of gentian violet, the staphylococci disappeared, the streptococci alone remaining in the urine. Fever and toxemia and all kidney symptoms disappeared, and the patient's life was unquestionably "saved."

In Cases 87, 97, 98, 99 and 100, great improvement was noted and fever and pain disappeared, but the record does not show that the urine was sterilized and the patient "cured." *B. coli* was present in three, streptococcus and staphylococcus were present in one, and cultures were not noted in two.

In all of the seventeen cases (cured or greatly improved), there was no doubt in the mind of the reporter that intravenous injection of mercurochrome-220 had been of great benefit. The dosage employed was generally high and multiple, only four times being 4 mg. per kilogram. Two or three doses of 4 or 5 mg. per kilogram were often employed.

Six cases were failures. In all of these cases fairly good doses were used, but only one patient received as much as three of 4 mg. per kilogram. *B. coli* was present in three, staphylococci in two. In two, cultures were not recorded.

In *B. coli* pyelonephritis, six were sterilized and three were not. In six in which the organism was not stated, *B. coli* was probably present; three were "cured," three not sterilized. In five cases with staphylococcus present, all were sterilized. The *B. coli* cases are thus shown to be variable in results; this corresponds to the great variation in resistance shown by Miss Hill in an exhaustive study of 150 strains of *B. coli.*

Among the "improved" cases are some which were finally sterilized by pelvic lavage. It seems probable that bacteria growing in the urine or urethra may not be reached by intravenous drugs in some cases and may require antiseptic lavage of the urinary reservoirs to sterilize them.

With eradication of the primary focus of infection, pelvic lavage and intravenous mercurochrome we believe that the great majority of pyelonephritic cases can be sterilized. Combined treatment is, therefore, indicated.

TABLE 8.—*Results of Intravenous Injection of Mercurochrome-220 in Thirty-Two Cases of Infection of Genito-Urinary Tract (Nongonorrheal)*

Group	Diagnosis	Total	"Cured" or Sterilized by Mercurochrome-220	Great Improvement after Mercurochrome-220	Failure
A	Perinephritic and retroperitoneal cases	4	2	2	..
B	Pyelonephritis	23	10	7	6
C	Cystitis and prostatitis	4	3	..	1
D	Chancroidal ulceration	1	1	..	..
		32	16	9	7

THIRTY-SEVEN CASES OF GONOCOCCUS INFECTIONS

TWENTY-SIX CASES OF GONORRHEAL URETHRITIS AND PROSTATITIS[84]

CASE 112.—*Acute gonorrheal urethritis. Intravenous injection of 5 mg. per kilogram of mercurochrome-220. Sterilization in twenty-four hours.*

A man, aged 23, weighing 180 pounds (81.6 kg.) was admitted Nov. 29, 1924, complaining of gonorrhea. He had had gonorrhea five years before and was still suffering from persistent urethral discharge. The present attack was of one week's duration. Examination showed profuse urethral discharge with marked edema and redness around the meatus. The slide smear showed pus cells and intracellular gram-negative diplococci in large number. The diagnosis was acute gonorrhea. The first glass of urine contained pus; the second and third glasses were clear. November 29, an intravenous injection of 44 c.c. of 1 per cent. mercurochrome-220, 5 mg. per kilogram, was given. By December 1, he had had very little reaction. He returned, and stated that the urethral discharge had almost disappeared. Examination showed a very slight mucoid discharge, which was composed only of epithelial cells and occasional leukocytes, but no gonococci. A second injection was given of 30 c.c. of 1 per cent.

84. Reference should also be made to Cases 138-149.

mercurochrome-220, 3.7 mg. per kilogram. December 2, there was very little reaction, very little urethral discharge, and no gonococci were present. December 6, 30 c.c. of 1 per cent. mercurochrome-220 (3.7 mg. per kilogram) was given intravenously. December 13, there was slight urethral discharge. No gonococci were present. The patient had had chronic gonorrhea, and it was probable that this was keeping up the urethral discharge, but it was thought wise to try one more large injection of mercurochrome-220 (44 c.c. of 1 per cent. solution, 5 mg. per kilogram). There was no reaction. December 17, the patient had had no return of gonococci in the urethral discharge. The diagnosis was old chronic urethritis for which he is receiving local treatment. The result of mercurochrome-220 in this case was simply to sterilize the urethra of gonococci.

CASE 113 (Whitman[85]).—*Acute gonorrhea. Five doses varying from 2 to 4 mg. per kilogram of mercurochrome-220 given intravenously. Disappearance of pus and infection.*

A white man, aged 22, admitted to treatment, March 10, 1924, had gonorrhea of sixteen months' duration. There was a history of cohabitation with a known infected woman three times afterward. There was a profuse discharge, showing myriads of gonococci and staphylococci. The kidney functional test gave 225 c.c., 35 per cent., in two hours. Five doses of mercurochrome, ranging from 2 to 4 mg. per kilogram of body weight, were given intravenously daily. There were moderate reactions after all injections. There was an astonishing decrease of pus secretion after the first injection, and gradual diminution thereafter. The absence of organisms was complete after the third injection. Stomatitis developed on the sixth day of treatment, and intravenous therapy was discontinued. Instrumentation and silver nitrate failed to secure any evidence of infection on and after the eighth day. No other treatment of any kind was given this patient, and he had remained free from any symptoms of gonococci infection up to May 3, 1924.

Dr. Whitman has published brief notes on eight other cases of gonorrheal urethritis, acute and chronic, in all of which mercurochrome was used intravenously with a result that the gonococci disappeared and, in all but one case, the urethral discharge left and did not recur. In most cases, he used several doses beginning with 2 mg. and going to 4 mg.; in one case he used 5 and in one case 7 mg. per kilogram, with reactions of varying intensity.

CASE 114 (Potter and Redewell[86]).—*Acute gonorrhea. Intravenous injections of 1 per cent. mercurochrome-220, five doses, from 10 to 25 c.c., at intervals of two days. Apparently cured.*

J. H. F., a second class seaman, was admitted to the sick list at the receiving ship July 18, 1924, with a profuse purulent discharge from the urethra in which gonococci were present. Routine 0.25 per cent. protargin strong injections and irrigations were ordered. At the end of four days, no improvement was observed, so all treatment was stopped. Injections of 1 per cent. mercurochrome-220 were made as follows: July 22, 10 c.c.; July 24, 15 c.c.; July 26, 20 c.c.; July 28, 25 c.c.; July 30, 25 c.c. All discharge stopped after he had received five injections, but the urine still contained a few shreds. August 3, 25 c.c. were injected. The patient complained of a mild stomatitis

85. Whitman, W. A.: Mercurochrome-220 Soluble Intravenously in Chronic Gonorrhea and Complications, J. A. M. A. **82**:1914 (June 14) 1924.

86. Potter, J. E., and Redewell, F. H.: U. S. Nav. M. Bull., to be published.

and a prickling sensation in the fingers. Mercurochrome treatment was stopped. A size 24 French sound was passed, followed by an irrigation of hot potassium permanganate, 1:5000, and instillation of 0.5 per cent. silver nitrate. August 8, a size 28 French sound was passed, followed by the same irrigation and instillation. August 10, the urine was clear and no smear was obtainable. The patient was discharged as cured.

Potter and Redewell used the same treatment in twenty-four cases which they tabulated as follows: All discharge stopped after the following number of injections: Two cases received two injections; five, two; five, four; five, five; seven, six or more injections, and four received three or more injections but still had a discharge. Other symptoms were improved.

All cases that had five or more injections did not have a recurrence of symptoms, but had a negative smear following instrumentation and deep instillation of 0.5 per cent. silver solution.

CASE 115 (Potter and Redewell[87]).—*Chronic gonorrhea of two years' duration. Intravenous injection of five doses of 1 per cent. mercurochrome-220, from 10 to 25 c.c. Apparently cured.*

F. A., a third class fireman, aged 25, was admitted to the sick list at the receiving ship, July 19, 1924, with a purulent discharge from the urethra in which gonococci were present. The patient had contracted gonorrhea two years before, and had had a chronic discharge ever since (over two years). The prostate was found to be apparently normal. The following treatments of 1 per cent. mercurochrome-220 were given intravenously with reactions as noted:

July 20	10 c.c.	No reaction
July 22	15 c.c.	No reaction
July 24	20 c.c.	No reaction
July 26	25 c.c.	Mild reaction
July 30	25 c.c.	Mild reaction
August 3	25 c.c.	Mild reaction

All discharge stopped after the fifth injection. The urine contained only a few shreds. The patient complained of a headache and malaise after the sixth injection, but did not develop stomatitis. August 4, sounds and 0.5 per cent. silver nitrate were used, and the urine still contained a few shreds. August 6, the urine was clear. August 8, sounds and 0.75 per cent. silver nitrate were used; a smear was negative for gonococcus. August 10, the patient was circumcised and, August 20, he was discharged as cured.

In all, Potter and Redewell treated eight cases of chronic gonorrheal infection of the urethra as follows:

One patient received two treatments of mercurochrome-220 intravenously. Four patients received five treatments. Three patients received six or more treatments.

All discharge stopped after the patients had received five or more injections. Three patients were cured. Three patients showed much improvement. Two patients were not improved.

CASE 116 (Potter and Redewell[87]).—*Prostatic abscess. Gonococci. Four intravenous injections of 1 per cent. mercurochrome-220, from 10 to 20 c.c. Disappearance of abscess, discharge and infection.*

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87. Personal communication from Drs. J. E. Potter and F. H. Redewell.

L. S. S., a second class seaman, aged 22, reported July 17, 1914, complaining of total retention of urine and painful vesical distention. He gave a history of gonococcus infection of the urethra, first acquired Feb. 20, 1923. He had had frequent recurrences. Examination revealed an enormous prostatic abscess and a urethral discharge with gonococci present.

After all attempts to make him void naturally had failed, the patient was catheterized to relieve vesical tension. No further catheterization was necessary. The following injections of 1 per cent. mercurochrome-220 solution were administered intravenously: July 19, 10 c.c.; July 21, 15 c.c.; July 23, 20 c.c., and July 25, 20 c.c.

Prostatic massage of increasing force was followed by irrigation with hot potassium permanganate, 1:5000, given every other day. All discharge from the urethra stopped after the third intravenous injection, but expressed secretion from the prostate and seminal vesicles still contained 100 white blood cells to the field, and gonococci were present. After six injections had been given, the patient reached mercurochrome saturation and this treatment was discontinued. August 11, the size of the prostate was greatly reduced although the right lobe was still indurated. August 18, the prostate was normal in size and firm in consistency. Expressed secretion contained only an ocasional pus cell. The urine was free from shreds. Instrumentation and injection of a 0.5 per cent. silver solution did not produce a return of symptoms nor a positive smear. The patient was discharged as cured.

Potter and Redewell had eleven cases of acute prostatitis which were treated with mercurochrome-220 intravenously. All cases showed improvement as follows: One patient received three injections; three, four; three, five, and five, six or more injections. One patient with prostatic abscess was completely cured after six injections. One patient with prostatic abscess was much improved, with marked amelioration of symptoms, but still had 50 white blood cells to the field.

Case 117 (Warterfield[88]).—A man, aged 36, had chronic gonorrhea and prostatitis. There were gonococci on the slide and in the culture. Two intravenous injections of 10 c.c. of 1 per cent. mercurochrome-220 were given. When the prostatic cultures were negative, 12 c.c. were given once. The patient then got drunk; there was no return of the discharge. Nevertheless, intravenous injections of 1 per cent. mercurochrome, 10 c.c., 12 c.c. and 14 c.c., were given. Recent cultures were sterile.

Case 118 (Whitman[88]).—The patient had chronic gonorrhea and prostatitis. Gonococci were present. Four doses of mercurochrome-220, 2.5 mg. per kilogram, were given intravenously. Stomatitis developed. Urethral injections were given for ten days. Then all tests were negative. The prostate was normal. The patient was apparently cured.

Case 119 (Whitman[88]).—The patient had chronic gonorrhea and primary syphilis, with extreme prepucial edema. There were multiple chancres of the glans penis and a copious discharge showing gonococci. Two doses of mercurochrome-220, 5 and 4 mg. per kilogram, were given intravenously at forty-eight hour intervals. Gonococci were absent after the fourth day. Complete healing of the lesions occurred. There has been no evidence of gonorrhea since. No local therapy was used.

88. Personal communication from Dr. F. E. Warterfield, Muskogee, Okla.

CASE 120 (Whitman[85]).—The patient had chronic gonorrhea. Gonococci were present. Intravenous injections of mercurochrome-220, 2 and 4 mg. per kilogram, were given. Stomatitis developed and the treatment was stopped. There was a termination of the discharge, and there has been no recurrence. No supplemental treatment was given.

CASE 121 (Warterfield[88]).—A man, aged 26, had gonorrheal epididymitis, accompanied by great swelling and pain. An intravenous injection of 10 c.c. of 1 per cent. mercurochrome-220 was given. The next day the patient was free from pain. Later, 23 c.c. and 15 c.c. were given. The secretions became normal, and there was no pus. The case was followed for two weeks, and the patient was apparently well.

CASE 122 (Warterfield[88]).—A man, aged 45, had acute gonorrhea, epididymitis and adenitis. An intravenous injection of 10 c.c. of 1 per cent. mercurochrome-220 was given. Four doses of 15 c.c. each were given. The discharge ceased. The swelling rapidly disappeared, and the urine became clear.

CASE 123 (Roeder and Judd[81]).—The patient had gonorrhea of four years' duration. An intravenous injection of 31 c.c. of 1 per cent. mercurochrome-220 was given. There was a "terrific reaction" followed by immediate disappearance of the discharge for the first time in four years. Two weeks later, although the discharge had not recurred, the patient was given a second injection. The urethral discharge did not reappear, although the case was followed for two months.

CASE 124 (Denny[89]).—The patient had chronic gonorrhea. Gonococci were present. Five doses, varying from 4 to 5 mg. per kilogram, of mercurochrome-220 were given. The discharge and the gonococci both disappeared. The patient also had local treatment. Final cure was reported. The case was followed for one month.

CASE 125 (Roeder and Judd[81]).—The patient had chronic gonorrhea of five years' duration, prostatitis, vesiculitis and epididymitis. He could hardly walk. An intravenous injection of 30 c.c. of 1 per cent. mercurochrome-220 was given. There was marked cessation of all signs and symptoms. The abscess of the epididymis was drained later. Seven days after the injection, the patient was up and about with a small morning discharge. No gonococci were present. The value of mercurochrome-220 in this case cannot be doubted.

CASE 126 (Case[58]).—A child, aged 4, who had a gonococcus infection, with complete retention of the urine and a prepucial abscess, was seen in convulsions. The abscess was incised. Five days later, an intravenous injection of 5 c.c. (4 mg. per kilogram) of 1 per cent. mercurochrome-220 was given. A second injection, the same dose, was given five days later, as well as local treatment. There was complete recovery.

CASE 127 (Warterfield[88]).—A woman, aged 36, had acute gonorrheal urethritis and endocervicitis. The temperature was 104. Smears were taken and the diagnosis verified. Gonococci were present. Three intravenous injections of 1 per cent. mercurochrome-220, 6 c.c., 8 c.c. and 10 c.c., were given. General improvement followed. The patient apparently got well, but this was not definitely stated.

CASE 128.—The patient had acute urethritis, gonococci being present, of three weeks' duration. Five intravenous injections of mercurochrome-220, 3 mg. per kilogram, were given at intervals of four and five days. There was a discharge in which gonococci were present. No benefit resulted.

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89. Personal communication from Dr. W. L. Denny, Baltimore.

CASE 129.—The patient had chronic gonorrhea and prostatitis. No gonococci were present. Four intravenous injections of mercurochrome-220, 2.3 mg. per kilogram, were given. One dose of 4.6 mg. per kilogram was given. Pus was still present in the urine and the prostatic secretion, but no gonococci. The result was indefinite.

CASE 130 (Whitman[85]).—The patient had chronic gonorrhea. Gonococci were present. Three intravenous injections of mercurochrome-220, 2.5 mg. per kilogram, were given. Severe stomatitis followed. The morning discharge persisted.

CASE 131 (Whitman[85]).—The patient had chronic gonorrhea. Gonococci were present. Four graduated doses of mercurochrome-220 were given. Stomatitis terminated the treatment. The pus discharge persisted. Local treatment was resumed for one month.

From the following four cases, three chronic gonorrhea and one acute, and with very small doses of mercurochrome-220, Lavandera[90] argues that mercurochrome-220 is without value (weights and frequency of treatments not given).

CASE 132 (Lavandera[90]).—A man, aged 34, with chronic gonorrhea of eight years' duration, had arthritis of the small toe. Four intravenous injections of 10, 14, 15 and 18 c.c. (percentage not given) of mercurochrome-220 apparently cured. Two weeks later he wrote that he had pain in the foot and the morning discharge as before.

CASE 133 (Lavandera[90]).—The patient had acute urethritis and epididymitis. Gonococci were present. Four intravenous injections of mercurochrome-220, 10, 11, 15 and 15 c.c. (percentage not stated) were given. Stomatitis developed. There was little improvement; gonococci were still present.

CASE 134 (Lavandera[90]).—A man, aged 19, had gonorrhea and epididymitis. Three intravenous injections of mercurochrome-220, 10, 11 and 15 c.c. (percentage not stated) were given. The patient was unimproved.

CASE 135 (Lavandera[90]).—A man, aged 22, had gonorrhea of two years' duration and prostatitis. A urethral smear was negative. Three intravenous injections of mercurochrome-220, 10, 15 and 15 c.c., were given on successive days. The condition was unrelieved.

CASE 136 (Whitman[85]).—The patient had chronic gonorrhea of twelve month's duration. Gonococci were present. Four daily doses of mercurochrome-220 (from 2 to 4 mg. per kilogram) were given intravenously. The gonococci disappeared. The morning discharge persisted. Mercurochrome-220 and urethral injections were continued.

CASE 137 (Whitman[85]).—The patient had chronic gonorrhea. Gonococci and staphylococci were present. Four daily doses of mercurochrome-220, 4 mg. per kilogram, were given. Pus and organisms were absent on the fourth day. The patient remained free from any evidence of gonorrhea. No other treatment was given.

In these gonococcus infections, there were twenty-six cases of urethritis of which twelve were cured. In the reports of these twelve cases,

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90. Lavandera, M.: Mercurochrome Therapy in Four Cases of Gonorrhea and Their Complications, J. A. M. A. **83**:1682 (Nov. 22) 1924.

it is positively stated that the discharge disappeared completely and, in most cases, that the urine was clear and gonococci absent. In all the reporter considered the disease eradicated. In only a few cases were provocative injections and cultures from the prostatic secretions obtained. Nevertheless, a clinical cure was apparently achieved in these twelve, or 46 per cent. of the cases. In four acute cases (gonococci noted), the dosage employed was: In Case 112, four doses of 5, 3.7, 3.7 and 5 mg. per kilogram; in Case 113, five doses of 2.4 mg. per kilogram; in Case 115, five doses of from 10 to 25 c.c. of 1 per cent. solution, and in Case 122, one injection of 10 c.c. and four of 15 c.c. All were sterilized.

In eight cases, chronic in duration, gonococci were noted in five and not in three. Only Case 123 was said to have been "cured" by one injection, 31 c.c. of 1 per cent solution. Two received from 2 to 5 mg. per kilogram and 2 and 4 mg. per kilogram (Cases 112 and 120). Case 121 received three injections of 1 per cent. solution, 10, 23 and 15 c.c. Two received four injections, Case 118, 2.5 mg. per kilogram each, and Case 116, from 10 to 20 c.c. of 1 per cent. solution. Case 115 had five injections varying from 10 to 25 c.c. of 1 per cent. solution, Case 117, six of from 10 to 14 c.c. of 1 per cent. solution. None of these twelve patients received any local treatment. In most of these twelve cases, the injections were given intravenously at intervals of forty-eight hours, and, in all but three, several treatments (from three to six) were given. In many cases, the gonococci disappeared after the first or second intravenous injection of mercurochrome-220, but additional treatments were given. While it is evident that multiple small doses (2 or 3 mg. per kilogram) may be effective, larger doses are to be preferred.

In five cases (Cases 124, 125, 126, 127 and 137), the reporter states positively that they were cured, but to be conservative we have classed them as greatly improved, because other treatment was sometimes employed. Large doses (from 4 to 5 mg. per kilogram) and several injections were generally used. In nine cases (34 per cent.), we have classed the results as failures. Four of these cases (Cases 132 to 135) were reported by Lavandera, who gave much smaller doses than have usually been necessary (from 10 to 15 c.c. of 1 per cent. solution, possibly only from 1.5 to 2 mg. per kilogram). Three were chronic cases without gonococci, one acute with epididymitis. Four other cases were chronic but with gonococci present: the dosage was small (Case 129, four of 2.3 mg. and 4.6 mg. per kilogram); the gonococci disappeared; pus was present. In Case 130, three doses of 2.5 mg. per kilogram were given, and in Case 136 four doses of 2.4 mg. per kilogram. In Case 131, the dose was not stated. In one acute case of four

days' duration, the patient received 3 mg. per kilogram five times at our clinic and gonococci were still present in the discharge.

Apparently gonococcus urethritis may in some cases be rapidly sterilized and all symptoms of disease disappear after several intravenous injections of mercurochrome-220, but doses of from 4 to 5 mg. per kilogram should be employed to secure results. With smaller doses, reaction may be avoided, but the patient may not be cured.

In a series of cases at the Brady Institute we have been less successful in destroying the infection in acute gonorrhea by intravenous injections of mercurochrome-220. In a few cases it has been done. Undoubtedly, urethral injections should also be used. For such complications as acute gonorrheal arthritis, the results of intravenous injections of mercurochrome-220 have been very good.

It seems probable that gonococci may be eradicated from the tissues and yet live and multiply in the urethra. On this account, antiseptic injections should also be employed. In dealing with this dread malady, every valuable weapon of offense should be used.

TWELVE CASES OF GONORRHEAL ARTHRITIS

CASE 138.—*Gonorrheal arthritis, urethritis and prostatitis, two intravenous injections of mercurochrome-220, 5 mg. per kilogram. Recovery.*

F. P., a man, was admitted to Brady Urological Institute, May 29, 1924, with gonorrheal arthritis of three days' duration, following an attack of specific urethritis which he had had for one month. On admission, the sternoclavicular, shoulder, knee, tarsal and metatarsal joints were swollen and exquisitely tender, especially on attempted motion. There also was considerable pain in the region of the lumbar spine. The temperature was 101, and the white blood cells totaled 9,600. There also was marked urethritis, prostatitis and vesiculitis. Studies of the urethral discharge revealed many gram-negative intracellular and extracellular diplococci.

In the afternoon of the day of admission, he was given an intravenous injection of mercurochrome-220, 5 mg. per kilogram. The temperature rose to 103 two hours after the injection, but was normal the next morning, when the patient was free from pain in the joints, even on motion and pressure. The patient, in fact, walked around the room without the aid of crutches and with only slight stiffness and no pain. Ten days later because of a gradual return of the arthritis, the foregoing dose of mercurochrome was repeated. On discharge, ten days following the last treatment, there was slight pain in the right hip and lumbosacral region as well as some stiffness of the joints. He was, however, able to walk fairly well with the aid of crutches. The prostatic discharge still contained many pus cells but no bacteria. The urine was also negative for infection. There was no urethral discharge. The patient was greatly improved.

CASE 139.—*Gonorrheal prostatitis and arthritis. Staphylococcus albus. Two intravenous injections of mercurochrome-220, 5 mg. per kilogram. Cured.*

G. A. W., was admitted to Brady Urological Institute, June 16, 1924, with a history of recurrent attacks of gonorrheal urethritis. The patient was brought

into the hospital suffering from marked gonorrheal arthritis of both knee joints and a prostatitis. Both knee joints were definitely swollen, and there was a definite limitation of motion. Culture of the urine and prostatic secretion showed *Staphylococcus albus.*

The patient was given an intravenous injection of mercurochrome-220, 5 mg. per kilogram. Three days later, he had almost perfect function of the left knee joint while the right was greatly improved. Cultures of the urine and prostatic secretion were negative. Twenty-seven days later, the foregoing intravenous treatment was repeated, and when the patient was discharged, six days later, he had practically complete function of both knees. The urine and prostatic secretions remained negative.

CASE 140 (Frontz[91]).—*Acute gonorrhea with arthritis involving left knee. Intravenous injections of 5 c.c. of 1 per cent. mercurochrome daily; after second day, 10 c.c., seven in all.*

A man, aged 24, weighing 200 pounds (90.7 kg.) had acute gonorrhea of three weeks' duration and arthritis of the left knee of four days' duration. The knee was tremendously swollen and painful; motion was considerably limited and the nocturnal temperature was 100. There was an acute urethral discharge, showing gonococci on culture. The urine was cloudy with pus. An intravenous injection of 5 c.c. of 1 per cent. mercurochrome-220 was given. The following day, a slight improvement was noted. The third day 10 c.c of 1 per cent. solution was given intravenously, and after that daily injections of 10 c.c. (1.1 mg. per kilogram). After eight days there was gradual but extraordinary improvement in the knee joint, which was only slightly larger than normal. It still showed a small amount of fluid in the periarticular tissues, but motion was complete without pain. The temperature was normal. The urethral discharge completely disappeared.

CASE 141 (Ferrer[92]).—*Gonorrheal arthritis of knee. Intravenous injection of mercurochrome-220, 5 mg. per kilogram. Recovery.*

G. R., aged 25 years, weighing 120 pounds (54.4 kg.), while hunting stuck a cactus needle into the left knee joint. This was followed by swelling of the joint, which lasted three days. Two weeks later, he acquired acute gonorrhea. Gram-negative diplococci were present in abundance. Six days later, the knee again became swollen and very painful, and he began to have fever. On admission, the temperature was 102; the white blood cells totaled 12,000; the knee was greatly swollen (size of a grapefruit), and the pain was excruciating. On the sixth day after entrance into the hospital, the swelling and pain being very great, he was given 5 mg. per kilogram of mercurochrome-220 (25 c.c. of 1 per cent. solution) intravenously at 10:30 a. m. At 1:30, he had a severe chill; he vomited twice and the temperature was 104. At 2:30 p. m., he was delirious; the temperature was 106.5. At 3:30 p. m., consciousness returned; the temperature was 106.5. The pain in the knee was less. At 6 p. m., the temperature was 104; the patient began to sweat; a bowel movement was stained red. At 7:30 p. m., the temperature was normal. The patient felt excellent. There was no pain at all in the knee. During the next four days, the temperature was normal and the pain in the knee had completely disappeared, but the swelling persisted. On the tenth day, the patient was able to move the knee and on the fifteenth day was out of bed. He soon was well.

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91. Personal communication from Dr. W. A. Frontz, Baltimore.
92. Personal communication from Dr. J. Ferrer, San Juan, Porto Rico.

CASE 142 (Warterfield[93]).—*Gonorrheal arthritis. Seven intravenous injections of small dosage of mercurochrome-220. Disappearance of arthritis and urethral infection.*[93]

A man, aged 29, weighing 150 pounds (68 kg.), exposed, June 27, 1924, on June 30 noticed a urethral discharge and used 10 per cent. protargin mild. July 3, examination showed a profuse discharge containing many intracellular gram-negative diplococci. The penis was much swollen, and there were enlarged lymphatic glands. Treatment was given with hot fomentations. July 5, the right elbow joint became swollen. July 6, the temperature was 101.5. There was great pain in the elbow joint, an increase of swelling, and a profuse urethral discharge. An intravenous injection of 1 per cent. mercurochrome-220, 1.4 mg. per kilogram, was given. Following this the patient had intestinal pain and severe diarrhea for several hours. The pain began to disappear and by the third day was entirely gone, and the swelling of the elbow was greatly reduced. At that time I decided to give him a second dose of mercurochrome-220, but owing to the severe reaction, he would not consent.

On the night of July 10, the right knee became involved, and he appeared in much worse condition than before. He had to be assisted to Dr. Warterfield's office owing to severe pain in the knee. The elbow had lighted up again. He was more than willing to receive the treatment, so he was given an intravenous injection of 12 c.c. of 1 per cent. mercurochrome-220, 1.7 mg. per kilogram. July 13, he walked into Dr. Warterfield's office unassisted, comparatively free from pain. He was given the same treatment, 12 c.c. of 1 per cent. mercurochrome-220 intravenously. There was hardly any reaction. Three days later, another injection of the same dosage was given, with no reaction. July 23, the same dosage was given; July 26 and July 29, 14 c.c. doses were given. There was no reaction following the last three doses. An interesting feature of this case was that the urine began to clear July 13 and by July 16 was absolutely clear and remained so until August 1, when a slight discharge appeared containing a few gram-negative diplococci. By August 8, the urine was again clear and has remained so since, all signs of infection having disappeared.

CASE 143 (Potter and Redewell[93]).—*Acute gonorrheal arthritis. Four intravenous doses of 1 per cent. mercurochrome-220, from 10 to 20 c.c. Discharged as cured.*

E. L., aged 26, an Italian laborer, was admitted to the genito-urinary clinic of the University of California Medical School, July 24, 1924, complaining of rheumatism and acute gonorrhea which he had acquired six weeks before. A smear was positive for gonococci. There were no urinary symptoms. Examination revealed gonorrheal rheumatism in the right wrist joint, which was much swollen and very painful. Hot irrigations of 0.5 per cent. protargin strong were given twice daily. The Wassermann reaction was negative. The condition did not improve.

July 28, the patient received 10 c.c. of 1 per cent. mercurochrome-220 intravenously; July 30, 15 c.c.; August 1, 20 c.c., and August 4, 20 c.c. There was a severe reaction.

August 5, the wrist joints showed much improvement. They had become movable without much pain. All discharge from the urethra had stopped. The

93. Dr. Warterfield reports seven other cases of gonorrheal infection with various complications, epididymitis, arthritis, etc., with some really remarkable results; these will be published in the Journal of Urology.

urine contained shreds. Mercurochrome treatment was begun again, August 9, with 15 c.c. of 1 per cent. solution given intravenously. August 11, the same dose was given. August 12, the urine was clear; the wrist joints were freely movable, normal in size and had no pain. He was discharged as cured August 24.

Four similar cases of acute gonorrheal rheumatism were treated by Potter and Redewell with mercurochrome-220 intravenously. One patient received four injections and one patient five injections, with much improvement. Two patients who received six or more injections were cured. Of all the cases reported in this article as having been treated with mercurochrome-220, the most striking results were thus obtained in these patients suffering with acute gonorrheal rheumatism.

Potter and Redewell also reported twelve cases of epididymitis and seminal vesiculitis, forty-eight cases of chronic prostatitis, thirty cases of chronic myalgia, two cases of cystitis and eight cases of synovitis in which they state that good results were obtained by mercurochrome-220 given intravenously. We have not space to record these interesting cases. They conclude that acute rheumatism synovitis, myalgia, neuritis, arthritis, acute gonorrheal urethritis, epididymitis, prostatitis and seminal vesiculitis cases will clear up rapidly on the intravenous administration of mercurochrome-220 soluble in a large number of the cases.

Case 144 (Warterfield[88]).—The patient had acute arthritis, the right sternoclavicular articulation and the right shoulder joint being seriously involved. Cultures yielded gonococci. No urethral treatment was given. Intravenous injections of 10 c.c. of 1 per cent. mercurochrome-220 were given five times. The arthritis and urethritis disappeared completely. The patient returned to work on the sixteenth day apparently cured.

Case 145 (Warterfield[88]).—*Acute gonorrheal arthritis. Four intravenous doses of mercurochrome-220. Cured.*

J. H., a white man, aged 18, was admitted with acute gonorrheal urethritis. He was given local treatment to use at home. Feb. 2, 1924, he returned with the right sternoclavicular joint very much swollen, very tender, painful and somewhat boggy. The right shoulder joint also was seriously involved. He supported the arm in a sling, and was unable to move the shoulder without very severe pain. The temperature was 100. He was given 10 c.c. of 1 per cent. mercurochrome-220. The reaction was moderate; there were nausea and copious stools. The next morning, the patient was free from pain and could use his arm.

Two days later, he returned for the second treatment. He had discarded the arm support and was free from pain, and the swelling had begun to subside. An intravenous injection of 10 c.c. of 1 per cent. mercurochrome-220 was given. The reaction was slight. February 14, the same dose was given. February 17, 12 c.c. was given. There was no reaction. By this time the tenderness, swelling and urethral discharge had disappeared, and the patient returned to work, February 18, and has had no return of either urethral discharge or the articular swelling or pain.

CASE 146 (Warterfield[88]).—A man, aged 29, had acute urethritis. Gonococci were present. He also had very severe arthritis of the elbow and knee. Intravenous injections of 1 per cent. mercurochrome-220, 10 c.c. and 12 c.c., were given three times, and 14 c.c. twice. Ultimate cure followed. The urethra was sterile. There was no discharge.

CASE 147 (Reed and Lum[25]).—A man, aged 39, had chronic urethritis, prostatitis and multiple arthritis. An intravenous injection of 30 c.c. of 1 per cent. mercurochrome-220 was given, and on the tenth day a second similar dose. The clinical improvement was reported as very satisfactory, though no definite facts were given.

CASE 148 (Warterfield[88]).—A man, aged 32, had chronic gonorrhea, prostatitis and multiple arthritis. Gonococci were present. An intravenous injection of 25 c.c. of 1 per cent. mercurochrome-220 was given. There was a very severe reaction. The following day, the patient was free from pain. A second injection was advised but refused.

Among the twelve cases of gonorrheal arthritis here recorded, in five the results are apparently cures, complete disappearance of the arthritis and initial infection. These cases are shown in Table 9. As seen here, gonococci were found in three, staphylococci in one, and in one case the organism is not stated.

The dosage in Case 139 consisted of two injections of 5 mg. per kilogram. The urethra, prostatic secretion and urine were completely sterilized, and the two badly involved joints became absolutely normal. In the other cases, from three to six injections of smaller dosage were employed, from 10 to 20 c.c. at intervals of two or three days. The results in these four cases (Cases 143, 144, 145 and 146) were excellent. In every case, the joint became practically normal and the urethral discharge and infection disappeared completely.

Four patients (Cases 138, 140, 141 and 142) may be classed as greatly improved. Gonococci were present in all in the urethral smear. Patient 138, with arthritis in the sternoclavicular, shoulder, knee and tarsal joints, had almost complete disappearance of arthritis. The urethral discharge disappeared and the urine became sterile after two doses of 5 mg. per kilogram. Patient 141, who received one dose of 5 mg. per kilogram, was said to have great improvement in the knee joint involved, but no note is recorded as to the infection. Patient 142 received seven small doses (1.4 mg. per kilogram) and was greatly improved. Patient 140, who received seven small doses of 10 c.c., had great improvement of extensive arthritis of the knee, the urethral discharge continuing and gonococci being present.

The deductions to be drawn from this series of four cases is that the treatment was inadequate, the dosage too small and the results unsatisfactory.

TABLE 9.—*Cases of Gonorrheal Arthritis Treated by Intravenous Injection of Mercurochrome-220 in Which Patient Was Cured*

Case	Urethral Discharge	Urine	Prostatic Secretion	Joints Involved	Temperature	No. Injections	Dosage, C.c. or Mg. per Kg.	Results
139	Negative	Staphylococcus	Staphylococcus	Both knee joints	No note	2	5 mg. per kg.	Urine and prostatic secretion sterilized; arthritis disappeared; function good
143	Gonococcus	Cloudy and contained shreds	No note	Right wrist very swollen and painful	No note	6	15, 15, 15, 20, 20, 10 c.c.	Urine became clear, wrist freely movable and normal in size; no pain
144	Gonococcus	Cloudy	No note	Right sternoclavicular region and right shoulder	No note	5	10 c.c.	Arthritis and urethritis disappeared completely
145	Gonococcus	Cloudy	No note	Right sternoclavicular region and right shoulder	100 F.	3	10, 10, 12 c.c.	Urethral discharge ceased and arthritis cured
146	Gonococcus	Cloudy	No note	Arthritis of right elbow and knee	No note	6	10, 12, 12, 12, 14, 14 c.c.	Ultimate cure; urethral discharge ceased

TABLE 10.—*Results of Intravenous Injection of Mercurochrome-220 in Thirty-Seven Cases of Gonorrhea*

Group	Diagnosis	Total	Apparently "Cured"	Improved	Failed
A	Urethritis and prostatitis	26	12	5	9
B	Arthritis	11	5	6	..
		37	17	11	9

FIVE CASES OF MULTIPLE ARTHRITIS (NONGONORRHEAL)[94]

CASE 149.—*Multiple acute arthritis; primary focus not discovered. Intravenous injection of 10 c.c. of 1 per cent. mercurochrome-220, approximately 1.5 mg. per kilogram. Apparently cured.*

N. S., aged 32, weighing about 140 pounds (63.5 kg.), was admitted to the genito-urinary department of Johns Hopkins Hospital dispensary, Dec. 1, 1922, with multiple acute arthritis involving both knees, both shoulders, both heels and the right elbow, of four months' duration. There was very great difficulty in walking. On admission, the temperature was 100. The joints noted were all swollen, tender, painful and with marked limitation of motion. Search for a focus was negative. The genito-urinary tract was normal. An intravenous injection of 10 c.c. of 1 per cent. mercurochrome-220, approximately 1.5 mg. per kilogram, was given three times weekly. Improvement began after the first treatment and the knees became normal. Both shoulders became normal after the fourth treatment, and the right elbow after four weeks. The condition at the end of a month was excellent. The arthritis was completely gone; all the joints were free, movable and without pain. Treatment caused no reaction except very slight stomatitis after one month. The urine was normal. There had never been any albumin or casts.

94. Reference should also be made to Cases 57, 58 and 185.

CASE 150.—*Chronic arthritis. Primary focus, prostatitis. Staphylococcus and streptococcus. Many intravenous injections of mercurochrome-220. Sterilization of urine and prostatic secretion. Great improvement in arthritis and joints.*

A man, aged 38, weighing 183 pounds (83 kg.) was admitted to Brady Urological Institute with advanced hypertrophic arthritis and chronic prostatitis. The urine on admission showed albumin and many streptococci. He had received six intravenous injections of mercurochrome-220, 3.5 mg. per kilogram, before coming to the clinic. Nov. 12, 1924, a dose of 4 mg. per kilogram was given, following which there was an increase of 1.5 in temperature. Six days later, the foregoing dose was repeated and was followed by a slight gastro-intestinal reaction. He was also given six doses of 3 mg. per kilogram with intervals of two days between injections, with little or no reaction. The urine at the end of the treatment showed few red blood cells but no casts and no bacteria. The phenolsulphonephthalein before treatment was 57 per cent. for two hours. After treatment, it was 58 per cent. for two hours. The final result was great improvement in the urine and the prostatic secretion became sterile. The arthritis was greatly improved, the pain gone.

CASE 151 (Walston[80]).—*Polyarthritis following tonsillitis. Intravenous injections of mercurochrome-220, 3, 5 and 1.5 mg. per kilogram. Recovery. Complete disappearance of rheumatism.*

H., a man, aged 23, weighing 153 pounds (68.9 kg.), had a history of repeated attacks of tonsillitis. When first seen by me he was well into the third week of an acute inflammatory rheumatism which followed a recent acute streptococcus tonsillitis. Many of the joints were swollen and inflamed and very painful. The fever ranged from 100.5 to 103.5. He could not be turned in bed without great pain. It was necessary to give him a hypodermic injection before he could be placed in the ambulance.

On entering the hospital, the white blood cells totaled 11,200, polymorphonuclears, 78 per cent. The urine contained albumin and many pus cells. He was given a special diet, hot packs, salicylates and 10 c.c. of milk protein without relief. On the fourth day, the condition was worse; the fever continued. He was given an intravenous injection of 20 c.c. of 1 per cent. mercurochrome-220, 3 mg. per kilogram, followed by a marked reaction. On the fifth day, 24 c.c., 5 mg. per kilogram, was given. There was a decided reaction. On the sixth day, 10 c.c. was given, followed by no reaction. On the following day, the patient was free from all symptoms and remained so. He was followed carefully for four months. The diagnosis was infectious type of acute inflammatory rheumatism due to the streptococcus from tonsillitis.

CASE 152 (Bland[95]).—*Multiple arthritis. Five intravenous injections of mercurochrome-220. Recovery.*

A woman with multiple arthritis of one week's duration was sent to the hospital and given from 12 to 15 c.c. of 1 per cent. solution of mercurochrome-220 intravenously each day for five consecutive days. At the end of that time she was well. She had no fever and no pain, was able to walk about, and in one week was at home. She received no treatment except mercurochrome-220 and used nothing locally except hot water bottles and cotton batting for the wrists and heels. Dr. Bland considered this result remarkable.

CASE 153 (Walston[80]).—The patient had inflammatory rheumatism following tonsillitis. Cultures yielded streptococcus. Many of the joints were swollen and painful. The temperature was 103.5, the white blood cells totaled 11,200.

95. Personal communication from Dr. Curtis Bland, Long Beach, Calif.

Urinalysis revealed albumin and pus cells. Three intravenous injections of mercurochrome-220, 3, 3.4 and 1.4 mg. per kilogram, were given. The following day, the patient was free from symptoms and remained so for four months afterward.

These cases of multiple arthritis, nongonorrheal in origin, are too few to draw any sweeping conclusions. The improvement, however, that came from intravenous injections of mercurochrome-220 was very striking in four cases. The disappearance of swelling, pain and restriction of motion in the joints in some of these cases was indeed very extraordinary and in some the relief was apparently permanent. The dosage varied but was always multiple. Very interesting arthritis cases described most fully under other lesions are Cases 57, 58 and 185.

MERCUROCHROME-220 ADMINISTERED INTRAVENOUSLY IN SKIN DISEASES

Among some of our early septicemia cases, serious infection of the skin, either in the form of erysipelas (streptococcus) or furuncles (staphylococcus) was present and disappeared with remarkable rapidity after intravenous injection of mercurochrome. We are now able to present a most interesting series of cases that show really wonderful results.

EIGHT CASES OF ERYSIPELAS

CASE 154 (Young and Birkhaug[96]).—*Erysipelas. Complicating septicemia, cervical adenitis and scarlet fever. Intravenous injection of mercurochrome-220, 7.5 mg. per kilogram. Recovery.*

A boy, aged 4 years, who had scarlet fever, developed extensive infection of the tonsils and glands of the neck and erysipelas of the face. The temperature was 105, the pulse 140. The patient was irrational. The erysipelas of the face was very extensive, covering both sides of the face and one ear; one eye was closed. The urine contained albumin, casts, pus cells and cocci. Cultures from the mouth and blood yielded *Streptococcus hemolyticus.* An intravenous injection of 15 c.c. of 1 per cent. mercurochrome-220, 7.5 mg. per kilogram, was given. No reaction followed. The next day the patient was markedly improved. A blood culture was sterile. The second day, the erysipelas and adenitis had almost completely disappeared; the temperature was normal. The blood was sterile. Following this, the patient made a rapid and uninterrupted convalescence. The erysipelas was gone. The urine became clear and normal. He was discharged from the hospital well on the tenth day.

This case is noteworthy as being the first demonstration and publication of the wonderfully rapid effect of intravenous mercurochrome in curing erysipelas.

CASE 155 (Smith[97]).—*Generalized erysipelas; "appeared moribund." Four intravenous injections of mercurochrome-220. Recovery.*

96. Young and Birkhaug (Footnote 19, eighth reference, Case 15 of article).
97. Personal communication from Dr. R. E. Smith, Grand Rapids, Mich.

An adult man, weighing 130 pounds (59 kg.), was admitted to the hospital, March 15, 1923, with extensive erysipelas of the face. The temperature was 104. The patient was treated for two weeks with antiseptic applications and opiates to relieve the pain. The temperature varied from 100 to 104 daily. March 29, the midnight temperature was 104.2. The patient was very weak, irrational and stuporous, and there was extensive erysipelas of the face, back, neck and arms and also a conjunctivitis. He had been running an extremely high temperature, was completely exhausted and appeared to be moribund when Dr. Smith decided to give mercurochrome-220 intravenously as a last resort. No reaction was observed, but the fever subsided in about twelve hours. Four injections were administered; the patient appeared to be free from any evidence of the disease. During this time, he had three definite relapses, which were followed by obvious improvement and practically normal temperature after administration of each of the three intravenous injections of 1 per cent. mercurochrome-220. Two weeks after the fourth injection of mercurochrome-220, the patient was practically well and in about one month was discharged from the hospital. Dr. Smith considered the result of mercurochrome-220 in this case wonderful.

The temperature charts showed the following injections of mercurochrome-220: March 29, at noon, the temperature being 102.7, 26 c.c. of 1 per cent. solution was given; at 5 p. m. the temperature was 104, and there were frequent stools. March 30, at 2:30 p. m., the temperature was 101.2, 30 c.c. of 1 per cent. solution was given; at 8 p. m. the temperature was 103.4, and there were frequent stools. April 1 at 5 p. m. the temperature was 98, 25 c.c. of 1 per cent. solution was given; at 7 a. m. the temperature was 101.4, and there was no diarrhea.

After this the patient had a normal temperature. No stomatitis or other reaction was recorded. The extensive wounds from the infection healed slowly. The patient was discharged, May 6, 1924.

CASE 156 (Abraham[89]).—*Erysipelas. Intravenous injection of mercurochrome-220, 5 mg. per kilogram. Reported cured.*

A man, aged 44, weighing 144 pounds (65.4 kg.), was admitted, April 5, 1924, to St. Mary's Hospital, Gallup, N. M., with typical erysipelas of the face. The temperature was 103. April 8, it was 102. Erythema had spread over the face, neck and chest. Both eyes were swollen and shut and both ears were markedly swollen. An intravenous injection of mercurochrome-220, 5 mg. per kilogram, was given at 8 a. m. The temperature rose to 102 at 2 p. m., and then dropped rapidly to normal during the night, and thereafter remained normal. On the following day, the patient was apparently cured, which was in less than twenty-four hours. April 10, all swelling had disappeared, and there was a marked scarring about the previous erythematous area. September 7, the patient was still well.

CASE 157 (Bland[95]).—*Erysipelas. Intravenous injection of 28 c.c. of 1 per cent. mercurochrome-220. Rapid disappearance.*

A woman, aged 24, with a history of several attacks of erysipelas, on May 4, 1924, had a new attack. Examination showed a typical erysipelas and extending to the right and left from the bridge of the nose. The lymphatic glands of the face and neck were enlarged, swollen and painful. She looked and felt very sick. The temperature was 103.6, the pulse 116. At 3 p. m. an intravenous injection of mercurochrome-220, 0.3 mg. in 30 c.c. of distilled water was given. In one-half hour the peculiar sensation in the skin and the pain were going and, in an hour, they were practically all gone. The swelling and pain that had been present in the

lymph glands in the neighborhood disappeared. Dr. Bland saw her the next morning and she was well. He called it uncanny. The patient had only recently had a long, serious attack of erysipelas and was amazed at the result of one dose.

CASE 158 (Roeder and Judd[21]).—*Erysipelas and cellulitis. Intravenous injection of mercurochrome-220. Rapid disappearance of lesions.*

W. G., a colored man, aged 19, single, with negative venereal history and Wassermann reaction, complained of malaise, fever, headache, a throbbing pain in the left tibial region and a marked swelling of the leg from the knee to the ankle joint. There was an ulcer over the tibia which had refused to heal since its traumatic origin about one month before. He had been confined to bed for one week, with gradual extension of a cellulitis throughout the deep structures. The appearance of the infection partially resembled erysipelas, but the marked involvement of the deep structures without the typical skin picture resembled more a cellulitis. There was a brawny induration throughout the entire leg with no fluctuation, a condition in which an incision did not seem advisable. There was no improvement after conservative treatment for a few days in the hospital, the temperature in the afternoon averaging 103, the pulse 120, and leukocytes 11,000. Four days after entering the hospital, the temperature had mounted to 104.8, with a marked involvement of the inguinal glands and general picture of sepsis. Thirty cubic centimeters of a 1 per cent. mercurochrome solution were given intravenously, followed by a rise in temperature to 105, a chill, vomiting and diarrhea, with a marked accentuation of the pain in the leg. In twelve hours, the temperature had dropped from 104.8 to 97.6, and did not again rise above normal. The general improvement from then on was steady, with a rapid absorption of the inflammatory products. The patient was dismissed six days after the mercurochrome therapy with the ulcer one-half the original size.

CASE 159 (Ruben[98]).—*Osteomyelitis and erysipelas. Intravenous injections of mercurochrome-220, 5 mg. per kilogram, and gentian violet, 5 mg. per kilogram. Recovery.*

A man, aged 54, weighing 150 pounds (68 kg.), had a multiple compound comminuted fracture of the right leg received four months before followed by infection and osteomyelitis. Examination showed extensive erysipelas. The patient was readmitted to the hospital. The leg showed evidences of erysipelas. The patient was extremely prostrated and in a critical condition.

Dr. Ruben said that he was not certain whether he was dealing with a cellulitis of the tissues, an acute osteomyelitis or both. He realized that if it was an acute osteomyelitis of the tibia and fibula, the bone must be opened to allow for drainage. Roentgenograms showed only bone rarefaction and excessive callus. If a cellulitis or erysipelas existed on the skin, trephining would carry surface infection to the bone.

It was decided to administer mercurochrome-220 intravenously; 5 mg. per kilogram were given. The temperature went from 100 to 104.5 in eight hours, and fell to normal three hours later. It remained below normal for twenty-four hours, when there was a chill and for two days a temperature between 101 and 102. The pain in the leg then subsided. The patient felt improved. After the temperature had been normal for thirty-six hours, the patient had a chill and the temperature rose to 104. Examination showed patches of erysipelas in new places above the knee. A blood culture at this time was negative. The white blood cells totaled 17,000. The urine contained albumin, casts and red blood cells. A culture from

98. Personal communication from Dr. S. A. Ruben, Washington, Pa.

the wound showed staphylococci and hemolytic streptococci. The patient was then given an intravenous injection of gentian violet, 5 mg. per kilogram (three days after the mercurochrome-220). The reaction was slight. The temperature soon dropped to normal, and the patient improved rapidly. The erysipelas disappeared. The wounds healed. The patient felt better immediately after each injection. Convalescence was satisfactory.

CASE 160 (Abraham[99]).—*Erysipelas. Intravenous injection of mercurochrome-220, 5 mg. per kilogram. Reported cured.*

A white man, aged 65, had an attack of erysipelas a year before admission. At first he was painted twice daily with 3 per cent. mercurochrome-220 and this seemed to limit the spread of the disease, but, several days later, a severe acute inflammatory rheumatism came on and lasted six weeks. Nov. 2, 1924, the patient again had typical erysipelas which started from the right nasal wing and, November 3, the right eye was closed. The patient was removed to the hospital where 1 per cent. mercurochrome-220, 5 mg. per kilogram, was given at 2 p. m. This was followed by a chill lasting six minutes, a rise in temperature in one

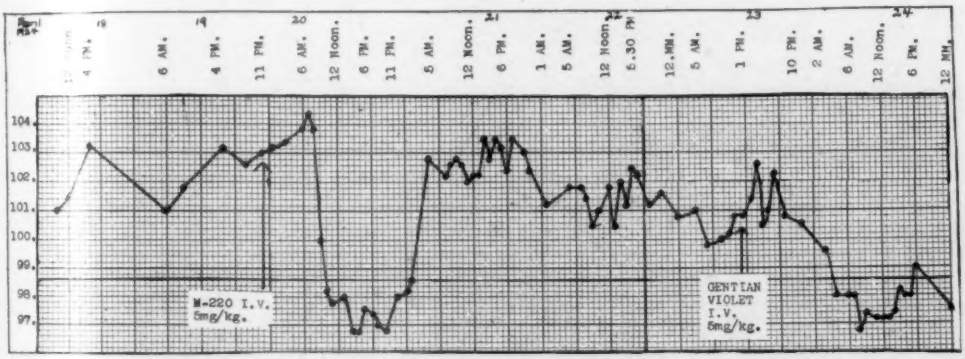

Fig. 13 (Case 159).—Temperature before and after intravenous injection of mercurochrome-220 soluble and gentian violet, each 5 mg. per kilogram, in case of osteomyelitis and erysipelas.

hour from 103 to 105, and a subsequent drop in six hours to 98. The following morning, the temperature was again normal and remained so. All swelling disappeared in forty-eight hours and scarring appeared. The ultimate result was that the patient was completely cured.

CASE 161 (Roeder and Judd[99]).—*Erysipelas. Intravenous injection of mercurochrome-220. Rapid disappearance.*

W. H. S., a woman, aged 26, developed an extensive erysipelatous infection in the wound twenty-one days after radical operation for carcinoma of the breast. The temperature was 104 and pulse 130 before an intravenous injection of 30 c.c. of 1 per cent. mercurochrome-220. This was followed by a chill and an increase of temperature to 106.6. In twelve hours the temperature had dropped to 100 and within twenty-four hours the erysipelas had faded remarkably. On the second day, the temperature became normal, and the redness of the skin practically disappeared.

99. The same patient is reported in Case 5.

In this series of eight cases with eight cures, we have some of the most striking results with intravenous injection of mercurochrome-220. The erysipelas varied in duration, type and extent. In some cases it was merely facial, in others very extensive, and in one involved the neck, body and arms. Several of these patients were desperately sick, the skin lesions were very extensive, and the temperature was high. The disappearance of the erysipelatous lesions was in almost all cases indeed extraordinary. The dosage in almost every case was high, about 5 mg. per kilogram, and in one 7.5. As a result, in six cases, only one injection was necessary to effect a complete cure with startling rapidity. One case received four, and one two injections. Not a single case of

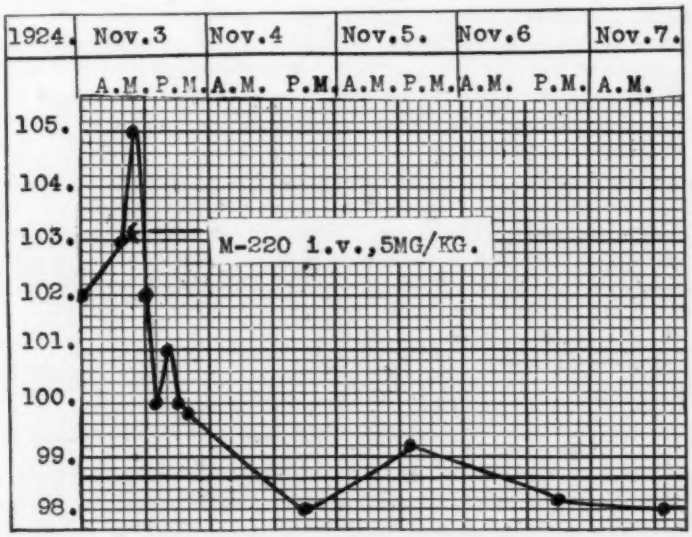

Fig. 14 (Case 60).—Temperature before and after intravenous injection of mercurochrome-220 soluble, 5 mg. per kilogram, in case of erysipelas.

failure in the treatment of erysipelas has reached us, and we feel that we can confidently state that the results obtained in Case 154 (which was the first published record showing the effect of mercurochrome-220 in erysipelas) have been no less brilliant than in the seven other cases here recorded.

FOUR NEW CASES OF FURUNCULOSIS AND TWO PREVIOUSLY RECORDED [100]

CASE 162.—*Extensive furunculosis of forearm. Interstitial cystitis, median bar. Intravenous injection of mercurochrome-220, 5 mg. per kilogram. Stomatitis. Rapid cure.*

100. Reference should also be made to Cases 24 and 29.

H. A. S., a man, aged 64, on whom a diagnosis of interstitial cystitis and median bar obstruction was made, entered Brady Urological Institute. A punch operation was indicated, but for several months he had suffered from extensive multiple furunculosis of the left forearm, and it seemed advisable to eradicate this infected area before attempting the punch operation. On the dorsal surface of the left forearm, midway between the wrist and the elbow, were five furuncles, the largest being 2 cm. in diameter, with definite core formation, from which *Staphylococcus aureus* was cultured.

The patient received an intravenous injection of mercurochrome-220, 5 mg. per kilogram. He developed a pronounced stomatitis after this treatment, which lasted a week. The furuncles began to dry on the day after the intravenous injection. Within eight days, all the furuncles had disappeared with the exception of the larger one, which healed later. The punch operation was successfully carried out and when the patient left, he was, for the first time in several months, free from boils. The operative wound had not become infected. The result was excellent.

CASE 163 (Frontz[101]).—*Furunculosis of lower extremities, very extensive. Culture: Staphylococcus aureus. Intravenous injection of mercurochrome-220, 4 mg. per kilogram.*

A man, aged 55, weighing 150 pounds (68 kg.), had an furuncle, involving the thigh and the lower legs, of six weeks' duration. On the lower left leg, there was a large ulceration, 3 cm. in diameter, covered with foul, gangrenous slough, and a marked reaction in the skin about the lesion. There was another lesion over the tibia of the same leg, and a similar lesion on the opposite leg, 1.5 cm. in diameter, a typical boil. On each thigh was a furuncle 1.5 cm. in diameter surrounded by an induration 5 cm. in diameter. Many other lesions, ranging from pustules to lesions 0.5 cm. in diameter, also were present. Cultures taken from two typical furuncles grew *Staphylococcus aureus.* An intravenous injection of 24 c.c. of 1 per cent. mercurochrome-220, 4 mg. per kilogram, was given. There was a moderately severe gastro-intestinal reaction; the following day, there was a marked improvement in all lesions. During the next five days, the improvement continued, and some lesions healed completely; others were composed only of granulation tissue. After a second dose of 4 mg. per kilogram, given five days after the first, the reaction was very slight. When last seen, four days after the second injection, all the small lesions had disappeared; the larger lesions were clean, with no suggestion of activity of infection, and were healing by granulation.

CASE 164 (Lanier[64]).—*Extensive furunculosis. Intravenous injection of 10 c.c. of 1 per cent. mercurochrome-220. Immediate improvement. Final cure.*

A girl, aged 16 years, with chronic asthma, had four or five boils on each arm, 3 or 4 inches (7 or 10 cm.) apart, six months after the skin tests for the asthmatic condition. An intravenous injection of 10 c.c. of 1 per cent. mercurochrome-220 was given, with almost immediate improvement. This was so great that a second injection was not given. There was final cure.

CASE 165 (Hopkins[77]).—*Carbuncle. Intravenous injection of 1 per cent. mercurochrome-220, 4.6 mg. per kilogram. Recovery.*

A. B., a man, aged 29, weighing 145 pounds (65.8 kg.), was admitted April 1, 1924, with a large carbuncle involving the entire lower lip, which was 3 cm. thick and everted. The temperature was 100.4. The patient was given 30 c.c. of 1 per cent. mercurochrome-220, 4.6 mg. per kilogram. There was little

101. Personal communication from Dr. W. A. Frontz, Baltimore.

reaction. This injection was repeated the following day. No operation was performed. The injection subsided rapidly, and he was discharged, April 13, with a practically normal lip. The mercurochrome-220 was of distinct benefit.

The six cases given above are the first to be recorded showing the really remarkable effect of intravenous injections of mercurochrome-220 in furunculosis. Cases 162 and 163, which were treated at this clinic, are excellent examples of the rapidity with which extensive staphylococcic boils may disappear. The case of the carbuncle was equally striking, as were cases Cases 24, 29 and 164 of generalized furunculosis. In one of our cases (Case 162) the entire group of boils disappeared after one injection of 5 mg. per kilogram. In Case 163, two injections of 4 mg. per kilogram were equally efficient. In the other cases, from 3 to 5 mg. per kilogram were used, from one to three doses being employed.

SEVENTEEN CASES OF CELLULITIS, ABSCESSES (SKIN) AND GANGRENE [102]

CASE 166 (Goldsborough [103]).—*Extensive cellulitis and sloughing. Streptococcus infection. Three intravenous doses of 10 c.c. each of mercurochrome-220. Recovery.*

A man, aged 19, received a severe traumatism of the leg. This was followed by a marked infection and, in twenty-four hours, he was brought to the hospital. Examination showed extensive skin slough from the ankle to the hip joint, with very severe infection. Subsequently, he had a large slough on the back, about the size of a dinner plate. During the stay in the hospital, he had three or four chills daily, very high temperature and sweats. A culture from the wound showed streptococcus. Blood cultures were sterile. Notwithstanding this, Dr. Goldsborough determined to give him an intravenous injection of mercurochrome-220, as recommended by us. Following an injection of 10 c.c. of 1 per cent. solution, the temperature went to 103, but rapidly fell to normal. On the following day, he was given a second injection and on the next day the third, each 10 c.c. of 1 per cent. solution. After that the temperature remained normal and he had no more chills; the leg rapidly assumed a different appearance. He was reported as eating heartily and getting well.

CASE 167 (Meriwether [104]).—*Extensive cellulitis. Septicemia. Intravenous injection of 10 c.c. of 1 per cent. mercurochrome-220. Recovery.*

The patient, a woman, received a blow in the face, Sept. 20, 1924. The upper lip was lacerated. September 24, Dr. Meriwether was called. The upper lip was bruised and swollen, with an indurated area extending beyond the angle of the mouth. Local applications were advised, and she was seen again at 4 p. m. By this time, she had become irrational, and complained of severe pains in her neck and around her heart. The swelling had greatly increased, and the indurated, reddened area had extended to within about an inch (2.5 cm.) of the left ear. The neck showed an extensive glandular enlargement on both sides. The temperature was 103.5 by mouth, pulse 120.

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102. Reference should also be made to Cases 3, 4, 7, 8, 38, 43, 157 and 158.
103. Personal communication from Dr. B. W. Goldsborough, Cambridge, Md.
104. Personal communication from Dr. B. M. Meriwether, Asheville, N. C.

At 5 p. m. she was given morphin, ¼ grain, atropin, 1/120 grain, and, a few minutes later, an intravenous injection of 10 c.c. of 1 per cent. mercurochrome-220. Twenty minutes later, she had a chill, lasting about seven minutes, after which she seemed much improved. At 10 p. m. (five hours after the injection), the condition was very much improved. The temperature was 100, pulse 108. At 4 a. m. she complained of intense cramps in the abdomen, and soon after passed by the bowels large quantities of a reddish colored fluid, containing a large amount of mucus. Morphin, ¼ grain, with atropin, 1/120 grain, was given for the intense pain, and later during the day, paregoric was substituted. The diarrhea was accompanied by nausea and vomiting. At 10 a. m. the temperature was 101, and at 3 p. m. 102. The swelling in the neck had decreased, and the glands were much smaller and less tender. The face also was much improved. A second injection of mercurochrome-220 was not given. The patient had an uneventful recovery. Two small localizations were incised and drained, both occurring in the upper lip. There was no phlebitis following the injection. During the first stages of the infection, a diagnosis of erysipelas was considered, but the general appearance and course was such that a final diagnosis of cellulitis with septicemia was made.

Case 168 (Adams,[26] Case 2).—*Traumatic paralysis, multiple abscesses and cellulitis. Culture: Streptococcus. Intravenous injection of 50 c.c. of 1 per cent. mercurochrome-220. Rapid healing.*

A man, aged 52, was admitted Sept. 28, 1923, with a fracture of the first lumbar vertebra, lower sacrum and coccyx, also a cord injury, as evidenced by paralysis below the level of injury and the usual urinary retention. He received conservative treatment. April 8, he began having a septic temperature. April 30, an abscess to the left of the anus formed and was drained. Cultures yielded streptococci. The process rapidly invaded the buttocks and the perineum, extending to the inguinal lymph nodes. Multiple incisions were made without controlling the sepsis. The blood showed no growth, and with the hope of raising the patient's resistance, 500 c.c. of fresh blood was given. Suppuration continued. May 8, he had a severe chill.

Fresh blood having failed, an intravenous injection of 50 c.c. of 1 per cent. mercurochrome-220 was given without reaction. The toxic symptoms subsided; the perineal and abdominal wall sinuses closed, and the sloughing in the regions of the buttocks and anus cleaned up. These results were obtained without reaction. The organism affected was the streptococcus.

Case 169 (Mann[105]).—*Large pharyngeal abscess. Operation. Sepsis. Intravenous injection of mercurochrome-220. Recovery.*

The patient was a negro man who had a very large pharyngeal abscess that appeared to have some connection with the vertebrae. It was feared that there was some necrosis of the vertebrae in this region. The abscess was drained, but the patient's condition grew steadily worse. When the temperature had reached 104, and there had been an increase in the amount of discharge from the abscess, he was given an injection of 23 c.c. of 1 per cent. mercurochrome-220. This was given at 6 p. m. on the fourth day of the disease. The temperature immediately dropped, and at no time after this one injection did it again reach 100. He was able to return to his home at the end of a week. At this time, all the discharge had ceased and the cavity appeared healthy.

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105. Personal communication from Dr. R. H. T. Mann, State National Bank Building, Texarkana, Ark.

CASE 170 (Kruse[106]).—*Multiple local infections. Streptococcus hemolyticus. Intravenous injections of 1 per cent. mercurochrome-220, 10 c.c., 12 c.c. and 19 c.c. Recovery.*

A girl, aged 17 years, was admitted to the University of California hospital, April 10, 1924, complaining of chills, fever and swelling and pains in the joints. She was very much prostrated and had a skin rash. The present illness had begun with a sore throat two months before. Since then the chills, fever, sweats and skin rash had developed. The temperature ranged between 101 and 103 daily; the joints had become swollen and painful. In March, the temperature rose daily to 105 and 106. This persisted for seven weeks until admission. A few days before admission, she had a small swelling back of the right ear, a suppurative gland. It was opened in the hospital. A culture yielded streptococci. April 12, the white blood cells totaled 12,400; April 24, 20,500. The polymorphonuclears were 88 per cent. The urine, April 14, had hyaline casts. A culture yielded *Streptococcus hemolyticus.*

April 22, the patient had been in the hospital for twelve days. The temperature had ranged daily between 37 and 41 C. The condition remained the same until April 23, when she received an intravenous injection of 12 c.c. of 1 per cent. mercurochrome-220. April 29, a dose of 19 c.c. was given. Following this there was an immediate drop of temperature below normal, and it thereafter did not go above normal during the nine days the patient remained in the hospital. She was discharged well, May 9. June 20, the patient was at home, had gained in weight, and was absolutely well.

Dr. Kruse considered the case an extremely interesting one. It was studied by a number of the staff of the University of California hospital. The exact cause of the general infection was not known. It was remarkable for the disappearance of the long continued fever after the third injection of mercurochrome-220.

CASE 171 (Wolff[107]).—*Gangrene of thigh following extensive traumatism. Intravenous injections of 20 c.c. and 15 c.c. of 1 per cent. mercurochrome-220.*

A man, aged 43, weighing about 135 pounds (61.2 kg.), was admitted in June, 1924, with extensive cellulitis and crepitus with evidence of extensive infiltration of the tissues of the right thigh following an injury which crushed the thigh. The wound was a longitudinal cut 4 inches (10.1 cm.) in length which extended through the skin and subcutaneous tissues on the outer portion of the thigh. Around this wound the tissues were indurated and crepitating over an area about 8 inches (20.3 cm.) in diameter, the upper limit being the right groin. The wound was suppurating violently. No bacteriologic studies were made. The evening temperature was 103.4, pulse 120, and respiration 28. The condition was extremely toxic.

Under ether, multiple incisions were made to enlarge the wound and open the undermined skin and subcutaneous tissues of the thigh, some of the incisions extending up to the groin. Numerous bubbles of gas came from these incisions. These were characterized by an extremely foul odor, which was recognized as typical of gas bacillus infections, Dr. Wolff having previously seen four fatal cases in which the patients had been given the same operative treatment that had just been given to this patient. Accordingly, it was decided to give this patient an intravenous injection of mercurochrome-220. This was done while the patient was still under ether, 20 c.c. of 1 per cent. solution being injected into the arm vein. This was done at 9 p. m. On the following morning the temperature

106. Personal communication from Dr. F. H. Kruse, San Francisco.

107. Personal communication from Dr. S. B. Wolff, Opelousas, La.

was 101, the pulse 100, and the general condition greatly improved. There was no reaction following the injection. Twenty-four hours after operation, the temperature was 100 and the condition greatly improved. Nevertheless, an intravenous injection of 15 c.c. of 1 per cent. mercurochrome-220 was given. No reaction followed. The condition the next day continued to improve. After this the wounds rapidly healed, and the patient had an uninterrupted and satisfactory convalescence.

The patient remained in the hospital for six weeks, during which time the deep wounds healed by granulation and were subsequently treated by skin grafts. During convalescence gas persisted in the subcutaneous tissues over an area from 5 to 6 inches (12.7 to 15.2 cm.) in diameter for four days after the operation. The patient six months later was entirely well. The diagnosis of gas gangrene was confirmed by Dr. O. P. Daly.

Dr. Wolff said that he felt positive that without the intravenous injection of mercurochrome-220 the patient would have died.

CASE 172 (Hopkins[72]).—A woman, aged 64, weighing 175 pounds (79.4 kg.) had tenosynovitis of the finger and cellulitis of the hand. Staphylococci were present. Incisions were made. An intravenous injection of 30 c.c. of 1 per cent. mercurochrome-220 was given and was repeated later. The patient was discharged well after amputation of the finger.

CASE 173 (Roeder and Judd[21]).—The patient had an infected hand and an enormous cellulitis of the forearm. Incisions were made. There was a persistent, brawny induration. An intravenous injection of 30 c.c. of 1 per cent. mercurochrome-220 was given. Twenty-four hours later the hand had decreased one-half in size. The skin became loose. Later the abscess was drained. Recovery followed.

CASE 174 (Slaughter[74]).—The patient had extensive lacerations of the right thigh and leg and infection. There was a septic temperature. Three intravenous injections of mercurochrome-220 of 2.7 mg. per kilogram were given. The swollen tissues gradually subsided and the wound became sterile. A successful skin graft was made. The patient was discharged well.

CASE 175 (Hopkins[108]).—A woman, aged 31, weighing 130 pounds (59 kg.) had a subpectoral abscess. She was very toxic and delirious. Cultures from the incision yielded *Streptococcus hemolyticus*. An intravenous injection of 30 c.c. of mercurochrome-220 was given. The delirium cleared in two hours. The pulse became slow. Nevertheless, she was given antistreptococcic serum. Additional incisions were made. The mercurochrome-220 was of definite value. The patient recovered.

CASE 176 (Bunten[20]).—The patient, following nephrectomy, had a large infiltrating area the size of the palm of the hand. An intravenous injection of mercurochrome-220, 1.4 mg. per kilogram, was given and repeated forty-eight hours later. There was severe salivation. The condition cleared up in a week.

CASE 177 (Case[88]).—The patient had cellulitis of the left leg following an old injury. The temperature was 103. An intravenous injection of mercurochrome-220, 3.8 mg. per kilogram, was given. In twelve hours, the temperature was 99.4. Rapid recovery followed.

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108. Hopkins, F. S.: Boston M. & S. J. **191**:732-736 (Oct. 16) 1924. This paper is accompanied by an interesting discussion, but the cases mentioned are too indefinite to incorporate here.

CASE 178 (Lanier[62]).—The patient had an infected finger and large axillary glands. An intravenous injection of 10 c.c. of 1 per cent. mercurochrome-220 was given. The next morning all symptoms were entirely gone.

CASE 179 (Hopkins[72]).—A man, aged 37, weighing 150 pounds (68 kg.), had diabetic gangrene of the toe, with infection of the leg. An intravenous injection of mercurochrome-220 was given. There was marked improvement. The infection disappeared. The patient got well after amputation of the leg at the ankle.

CASE 180 (Hopkins[72]).—A man, aged 63, weighing 165 pounds (74.8 kg.), had an infected wound after herniotomy. A culture yielded staphylococci. An intravenous injection of 30 c.c. of 1 per cent. mercurochrome-220 was given. After eleven days the wound was well healed. The value of the mercurochrome was doubtful.

CASE 181 (Hopkins[72]).—A man, aged 34, weighing 150 pounds, had a fracture of the skull, laceration of the brain and traumatic amputation of the left arm and right fingers. When the wounds were dressed, 30 c.c. of 1 per cent. mercurochrome-220 was used as prophylactic. The same dose was given again four days later. The patient died of convulsions. When the extent of his injuries is considered, it was surprising that he lived for twelve days and remained free from infection. The mercurochrome-220 may account for this.

CASE 182 (Hopkins[72]).—A man, aged 71, weighing 135 pounds (61.2 kg.), had a streptococcic cellulitis of the lower left leg. An intravenous injection of 30 c.c. of 1 per cent. mercurochrome-220 was given. No reaction followed. The dose was repeated. The patient died later.

CASE 183 (Bowman[25]).—*Acute skin eruption like psoriasis. Gentian violet and neo-arsphenamin failed. Three intravenous injections of mercurochrome-220, 5 mg. per kilogram. Recovery.*

A man, aged 24, had a history of fever suggesting *Streptococcus viridans* septicemia, but repeated blood cultures were negative. He finally developed a severe eruption similar to psoriasis. The Wassermann reaction was negative. He was given several injections of gentian violet, with no change in the temperature or condition. He was then given neo-arsphenamin, 0.75 gm., but without result. Three intravenous injections of mercurochrome-220, 5 mg. per kilogram, were then given (interval not stated). The temperature, which had been high, became normal. The eruption disappeared and the patient made an uneventful recovery.

In these eighteen cases, we have grouped together a great variety of superficial and deep infections of the skin, subcutaneous tissues and soft parts. The pathologic process has been very varied. The streptococcus was isolated from five cases, and staphylococcus from two. In the others no record is at hand. The clinical description, however, justifies the diagnosis in practically every case. In the first eleven cases here recorded (Cases 166 to 178), the rapid disappearance of the lesion and the recovery of the patient are sufficiently definite to class the patients as cured. In several of these, abscesses were present, in others only a brawny induration of deep cellulitis of the skin; in one, Case 171, there was a definite, extensive gangrene of the thigh.

The dosage employed in these eleven cases was as follows: In six only one dose was used, varying from only 10 c.c. of 1 per cent. solution to 6 mg. per kilogram. In the other four cases, two or three injections were used, varying from 1.5 to 3 mg. per kilogram. In four cases, the patients recovered and the local infection seemed to be greatly improved as a result of the intravenous injections. In each of these cases 5 mg. per kilogram was used. In one case (Case 180), the effect of the injection was doubtful and in two cases (Cases 181 and 182) the patients died.

Summarizing, we can safely say that in fifteen of the eighteen cases of cutaneous and subcutaneous infections and abscesses the patients have been markedly improved by the use of mercurochrome-220, the effect of which in most cases was indeed very striking and rapid.

TWO CASES OF PEMPHIGUS

We take pleasure in quoting some observations by Schamberg:[109]

For the last year or so we have had an unusual incidence of pemphigus in my clinic. I have had about twelve patients, all of which died save one.

We have made exhaustive blood studies of these patients and have isolated from the blood streptococci and, in one or two cases, bacilli. Pemphigus presents all the evidences of infectious disease and has been fatal in about 90 per cent. of the cases. Indeed, in some cities, it has been fatal in almost 100 per cent.

Greenbaum recently suggested a trial of mercurochrome-220. He tried it on an extensive case of pemphigus in Polyclinic Hospital and with a most astonishing result. A man who was covered with blebs from head to foot is now completely free of lesions and shows merely the pigmentation marking the sites of the former eruption. He received only three injections, one of which was about 34 c.c. of a 1 per cent. solution.

I have used this preparation in 5 c.c. doses on a case of beginning pemphigus of the lips and mouth in my private practice. After two injections the blebs on the lips, which had persisted for five months, completely disappeared.

This extensive case was shown by Drs. Schamberg and Greenbaum before the Tri-City Dermatological Association meeting, Oct. 14, 1924.

We quote from another letter:

The patient with pemphigus given intravenous injections of mercurochrome-220 which caused such a marvelous disappearance of an extensive eruption has not continued to show the improvement which we had hoped would be achieved. In spite of the further use of the drug, new crops have appeared and the patient is now almost in extremis. I have had two cases in private practice with most satisfactory results.

Case 184 (Schamberg[109]).—A woman, aged 30, for five months had presented recurring blebs on the lips with an abortive eruption on the backs of the hands, and later a few lesions in the mouth, which I believed to be a beginning case of pemphigus. She received thirty-five intravenous injections of sodium cacody-

109. Personal communication from Dr. J. F. Schamberg, Philadelphia.

late and a similar number of subcutaneous injections of a proprietary thromboplastic preparation without effect. After the first intravenous injection of 5 c.c. of 1 per cent. mercurochrome-220, relief immediately set in, and after the second injection the eruption disappeared. During the last two months, there has been no tendency to relapse.

CASE 185 (Schamberg[109]).—A woman, aged 50, was troubled for two years with stomatitis areata ulcerosa. The tongue and buccal mucous membrane was the seat of large superficially ulcerated patches covered with pseudomembrane. Resisting all treatment received, the lips became involved, the lower being covered with a heavy blood crust. Dr. Schamberg felt that this might be an atypical onset of pemphigus. He administered 1 per cent. mercurochrome-220 intravenously, in doses of from 5 to 10 c.c. The eruption on the lips promptly cleared up, and the mouth was greatly improved, although a few small patches still remained. She is still under treatment and improvement is progressive.

Dr. Schamberg said that he did not believe that anyone could classify exactly the pathogenesis of the latter type of condition. It seemed to him most interesting that it should have yielded to the intravenous use of mercurochrome-220.

While the cases of pemphigus are yet too few and too indefinite to warrant positive deductions, we feel that Dr. Schamberg and his associates have certainly demonstrated most interesting results in these cases from the intravenous injections of mercurochrome-220.

TABLE 11.—*Result of Intravenous Injection of Mercurochrome-220 in Thirty-Two Cases of Skin Infections*

Group	Diagnosis	Total	Cured	Effect of Mercurochrome-220 Improved	Doubtful	Failed
A	Erysipelas	8	8	..	..	..
B	Furunculosis	4	4	..	..	..
C	Cellulitis and abscesses	17	11	3	1	2
D	Psoriasis-like eruption and pemphigus	3	1	2	..	..
		32	24	5	1	2

OSTEOMYELITIS

The cases of osteomyelitis have been classified under other headings. References should be made to Cases 7, 21, 23, 25, 26, 27 and 28.

THREE CASES OF PHLEBITIS[110]

CASE 186 (Slaughter[74]).—A woman had phlebitis with severe pain in both legs following delivery. The temperature was 101.4. Six intravenous doses of 1 per cent. mercurochrome-220, 3.3 mg. per kilogram, were given. The temperature went to normal. The pain was practically gone. She was discharged in good condition.

CASE 187 (Reed and Lum[55]).—The patient had multiple abscesses of the soft parts, arthritis, thrombophlebitis and bronchopneumonia. Pus from the abscess showed nonhemolytic streptococci. Blood cultures were negative. An intravenous injection of 35 c.c. of 1 per cent. mercurochrome-220 was given. No

110. Reference should also be made to Cases 30 and 44.

reaction followed. The second day, 40 c.c. was given. Diarrhea was marked. The sixth day 28 c.c. of 1 per cent. gentian violet was injected intravenously. He subsequently recovered.

CASE 188 (Piper [11]).—The patient had thrombophlebitis. He received a dose of mercurochrome-220 (amount not stated), and showed improvement, but eventually died.

In a recent report, Schallenberger has presented a number of cases of thrombophlebitis in which intravenous treatment has been used, gentian violet being employed in the majority of cases, mercurochrome-220 in others. The details have not yet been furnished us, but the results, we understand, are considered very interesting and worthy of further trials.

MISCELLANEOUS INFECTIOUS AND CONTAGIOUS DISEASES

As stated before, it has been our aim in this paper to bring together a complete record of all the cases in which mercurochrome-220 has been used intravenously. In pursuing this plan, we have naturally found it necessary to record here isolated instances in which the drug has been employed in a small number of varied contagious and infectious diseases, such as typhoid fever, poliomyelitis, meningitis, encephalitis, Rocky Mountain spotted fever, bubonic plague, scarlet fever and tuberculosis, with secondary infections. These cases are too few in number to warrant drawing any positive deductions as to the value of mercurochrome-220 and the dosage in which it should be employed in these cases, but the clinical records are, in some instances, of great interest, sufficient to warrant much further experimental and clinical work along these lines.

FIVE CASES OF TYPHOID FEVER

Our experimental work with mercurochrome-220 given intravenously and by mouth and the demonstration that the bacterial content of the feces was greatly lowered by the use of mercurochrome-220, and later that the bile contained mercurochrome-220 in sterilizing strength, and that artificially produced typhoid cholecystitis could be cured by mercurochrome-220 given by mouth or intravenously, led us to hope that mercurchrome-220 might be found of value in typhoid fever. We have received brief reports of seven cases in which this has been carried out. While the reports are not so complete and detailed as we should like, they are still of considerable interest and worthy of study. The drug was used in typhoid fever independently by Drs. Bond and Barrier, Little Rock, Ark.; Redfern, Winston-Salem, N. C., and Slaughter, Bogalusa, La., in July, 1924. The only published report is that of Bond and Barrier,[111] who say:

111. Bond, S. P. and Barrier L. F.: J. Arkansas M. Soc. **21**:71 (Sept.) 1924.

Seeing reports in several journals of the use of mercurochrome-220 intravenously in septicemia, septic bacteremia, we began in 1924 the use of mercurochrome-220 intravenously. We have used the drug in twelve cases of typhoid fever, and by its use have lessened the stay of the patient in the hospital from one-third to one-half the average time.

One case is cited:

CASE 189 (Bond and Barrier[111]).—*Typhoid fever. Three intravenous doses of 1 per cent. mercurochrome-220, 5 c.c., 10 c.c. and 18 c.c. Recovery.*

A man, aged 30, weighing 130 pounds (59 kg.) was admitted July 14, 1924, with provisional diagnosis of typhoid fever. The Widal test was negative until the afternon of July 16, when the laboratory report showed a slight positive reaction. An intravenous injection of 5 c.c. of 1 per cent. mercurochrome-220 was then given. This was followed by a short decline in temperature from 103.4 to 100. July 18, the temperature having risen to 103.8, an intravenous injection of 10 c.c. of 1 per cent. mercurochrome-220 was given. The reaction was sharp. Six days later, a third injection of 18 c.c. was given. This was followed by a sharp reaction with a temperature of 104; the pulse was only slightly accelerated; the respiration was unchanged. This was followed by a sharp decline of temperature to 97, after which the temperature remained normal and did not rise above 99. The patient was discharged well fifteen days later.

CASE 190 (Linn[112]).—*Typhoid fever. Two intravenous injections of mercurochrome-220, 2.6 and 4.4 mg. per kilogram. Recovery.*

A man, aged 19, weighing 125 pounds (56.7 kg.), was seen, Aug. 16, 1924, with a temperature of 103. He had been feeling bad for one week and had had fever for one day. August 21, a Widal test was positive. The temperature for three days was between 101 and 103. The diagnosis was typhoid fever.

August 22, at 9:45 a. m. an intravenous injection of 15 c.c. of 1 per cent. mercurochrome-220 was given. This was followed by vomiting, chill and a temperature of 105.6. The temperature declined rapidly and reached 98.6 at 9:30 p. m. There were five bowel movements. The next day the highest temperature was 100.4. On the following day, it reached 102.8.

August 26, at 9:30 a. m. an intravenous injection of 25 c.c. of 1 per cent. mercurochrome-220 was followed by vomiting, chill and a temperature of 104.6. After this the temperature rapidly declined, reaching 98 at 10:30 p. m. During this day there were two bowel movements, but no intestinal disturbance. The day following each mercurochrome treatment, the condition was markedly improved.

After the second injection, the temperature remained practically normal, and the patient convalesced quickly. The patient remarked on the great improvement after each injection, and was glad to take the second dose. Dr. Linn felt that this treatment was of great benefit in this case, and said that he would use a larger initial dose the next time.

CASE 191 (Slaughter[74]).—*Typhoid fever. Ten intravenous doses of mercurochrome-220, each of 3.2 mg. per kilogram. Recovery.*

A colored man, aged 23, weighing 135 pounds (61.3 kg.), was admitted to the hospital July 12, at 3 p. m. The temperature was 103.8, the pulse 100 and

112. Personal communication from Dr. H. P. Linn, Paducah, Ky.

respiration 30. He complained of pain in the head and back. The temperature during the night reached 105. He had a positive Widal test. July 14, the temperature was 104.4.

The patient was given ten doses of mercurochrome-220, each 3.2 mg. per kilogram, between July 14 and August 19. After every dose of mercurochrome-220, the temperature went to normal. August 7, it began going up and, August 11, it reached 104. At this time he was given the ninth dose of mercurochrome-220. The temperature dropped to 97.5. He ran a temperature around 100 each suceeding day until August 19, when he was given the last dose of mercurochrome-220. The temperature went to normal.

Dr. Slaughter said that he was convinced after treating this case that the dosage was too small. He thought that if the patient had been treated with 23 c.c. of mercurochrome-220 for each 100 pounds of body weight, the temperature would have been controlled earlier. The temperature chart showed conclusively that mercurochrome-220 had a very beneficial effect on this patient.

This case is principally interesting in demonstrating that in one month ten doses of mercurochrome-220 can be given intravenously without marked reaction or ill effect. The effect of the drug on the disease cannot be stated positively.

Slaughter reports two other cases of typhoid fever in which mercurochrome-220 was used, in one of which stomatitis occurred after a single injection of 2.9 mg. per kilogram. Both patients recovered.

CASE 192 (Slaughter[74]).—The patient had typhoid. The Widal test was positive. Three injections of mercurochrome-220 were given intravenously (dosage not given). There was a rapid fall in temperature and recovery.

CASE 193 (Slaughter[74]).—In a case of typhoid, a Widal test was positive. An intravenous injection of 20 c.c. of 1 per cent. mercurochrome-220 was given. The dose was repeated the next day. The reaction was slight. Rapid recovery followed.

The number of cases here recorded (seven) is much too small from which to draw any deductions, except to say that in these cases and in the twelve treated by Bond and Barrier there was no evidence that mercurochrome-220 injected intravenously produced harmful reactions in cases of typhoid fever. Our demonstration that the drug is eliminated in sterilizing quantity through the gallbladder and that often when given by mouth it has pronounced effect on the bacterial content of the stools, taken in conjunction with these clinical reports is sufficiently impressive to warrant an extended trial of mercurochrome-220 in typhoid fever. The dosage employed by Bond and Barrier was 10 c.c. of a 1 per cent. solution.

In Case 190 the initial dose was 15 c.c. of 1 per cent. solution (2.5 mg. per kilogram). Four days later, 4 mg. per kilogram was given without reaction and with marked effect on the temperature and course of the disease. In Case 191 ten doses of about 3.2 mg. per kilogram were given in one month, but Slaughter remarks that he believes larger doses should have been employed.

It is impossible to draw any positive deductions as to dosage and frequency. Enteric coated mercurochrome pills, which we have shown to

have marked effect in reducing the intestinal flora, may yet be found as satisfactory as intravenous injections. We await with great interest a careful study of the clinical results with mercurochrome-220 in a long series of typhoid cases and cases of typhoid carriers.

TWO CASES OF ACUTE ANTERIOR POLIOMYELITIS

CASE 194 (Walston[80]).—*Acute anterior poliomyelitis. Five intravenous injections of mercurochrome-220, 2.6, 0.6, 1.3 mg. per kilogram. Rapid recovery. No paralysis.*

T. M., a man, aged 19, weighing 165 pounds (74.8 kg.) was taken sick, May 26, 1924, with chilliness, fever, aching and nasopharyngeal symptoms. He remained in bed for four days at home, felt improved, and went back to work for six days. He was again taken ill, with stiffness in the neck and back and some pain in the legs, with severe headache. He commenced to vomit, and was very drowsy and inclined to sleep. Then there was gradual development of flaccid paralysis until he was unable to move either leg. Paralysis of the sphincter of the bladder was complete. Inguinal hernia developed. The condition remained the same for nine days. A diagnosis of acute anterior poliomyelitis in this case was positive.

Relying on Rosenow's theory that the disease is a form of streptococcus infection, Dr. Walston decided to use mercurochrome-220 intravenously. The patient was given an intravenous injection of 20 c.c. of 1 per cent. mercurochrome-220. The reaction was moderate. The next day the same dose was repeated. Then for three days he was given from 5 c.c. to 10 c.c. The improvement was rapid. In one week, he went home walking unassisted to and from a taxicab. In another week, he was at work without any remaining evidence of paralysis.

CASE 195 (Walston[80]).—*Anterior poliomyelitis. Two intravenous injections of mercurochrome-220, 5 mg. per kilogram. Recovery.*

M. P., a school girl, aged 14 years, weighing 72 pounds (32.7 kg.), had never had any illness or injury. She was taken sick, June 5, 1924, with coryza, pharyngitis, fever, chill, aching and severe headache. She stayed at home for ten days and then went to school part of a day. She had to be excused on account of illness. Two days later, she was unable to get out of bed on account of almost complete paralysis of both legs. The patellar reflexes were gone in the left leg and nearly so in the right. The legs were covered with purpura spots from 3 inches (7.6 cm.) above the knee to the feet. The paralysis remained for four days when she was given an intravenous injection of 16 c.c. of 1 per cent. mercurochrome-220, 5 mg. per kilogram. The same dose was repeated the following day. The day following this, the patient had regained almost complete use of the limbs and made a rapid and uneventful recovery. Dr. Walston felt sure of the diagnosis of acute anterior poliomyelitis.

TWO CASES OF EPIDEMIC ENCEPHALITIS

CASE 196 (Vischer[113]).—*Epidemic encephalitis. Intravenous injection of mercurochrome-220. Recovery.*

V. J., a boy, aged 16, weighing 140 pounds (63.5 kg.), April 6, 1924, developed measles. April 11, there was complete retention of urine, associated with

113. Vischer, J. W.: Epidemic Encephalitis Treated with Mercurochrome-220; Two Cases, N. W. Med., June, 1924.

mental confusion and emotional depression. The temperature was 102. April 25, the patient was admitted to the hospital. He appeared very sick. His speech was low. Temperature, pulse and respiration were normal. Examination showed exaggerated tendon reflexes and a bilateral ankle clonus. The plantar reflex was lively. There was no Babinski reflex. Leukocytosis was 12,000. The Wassermann reaction and urine examination were negative. April 30, the condition was very critical. A bad prognosis was given. The patient had failed rapidly in the last three days. He was unable to sleep. He spoke with difficulty and indistinctly. Examination showed marked spasticity of all the skeletal muscles, which was so marked on the left that he was unable to move the arm or leg. There was bilateral ankle clonus and a Babinski reflex on both sides. The neck was stiff. Kernig's sign was positive. The pupils were widely dilated but reacted to light. Leukocytosis was 16,000. Spinal fluid was withdrawn, under somewhat increased pressure; there was no pleocytosis. The globulin and spinal Wassermann reactions were negative. He could not drink from a glass, as the lips were spastically contracted and the tongue stiff.

April 30, at 8 p. m., an intravenous injection of 10 c.c. of 1 per cent. mercurochrome-220, 1.5 mg. per kilogram, was given. The next morning, the patient was much improved; he could speak quite clearly and take fluids and move the left arm easily. That evening an intravenous injection of 8 c.c., 1.2 mg. per kilogram, was given. The ankle clonus and the Babinski reflex disappeared on the second day, and the generalized spasticity and speech difficulty rapidly improved. Within a week, he was perfectly quiet and happy. He left the hospital, May 11, twelve days after the first injections of mercurochrome-220, apparently well. The first day in the hospital, the pulse varied between 108 and 140, but four days later it was 74. The highest temperature recorded was 99.6 on the third day.

Case 197 (Vischer[118]).—*Epidemic encephalitis. Intravenous injection of mercurochrome-220. Recovery.*

F. W. B., aged 51, weighing 140 pounds (63.5 kg.), was seen, May 12, 1924, complaining of inability to talk, restlessness and pain and stiffness of the legs. The temperature was 98, pulse 70 and respiration 18. Leukocytosis was 6,500. The urine examination and Wassermann reaction were negative. The face had a wild, staring expression like a hideous mask. The pupils were large, but reacted to light. The reflexes were normal, but there was a marked cutaneous reaction and deep hypersensitiveness. The movements of the patient were slow and clumsy. Physical examination was otherwise negative. He was removed to the hospital at noon.

He was given an intravenous injection of 10 c.c. of 1 per cent. mercurochrome-220. At 4 p. m., he started to improve and began to talk, but could not drink water or medicine. At 8 p. m., he was more improved in speech and mentally clearer, but still unable to understand commands. The next morning, the change in the condition was spectacular. He was able to converse fairly intelligently, although he was still somewhat confused. He took fluids easily. Twenty-four hours later, the sensorium was perfectly clear and recovery was complete, except that the facial expression was still masklike. The latter disappeared during the next twenty-four hours, and the patient was discharged from the hospital apparently well, May 15, three days after the injection of mercurochrome-220. The pulse varied from 88 the first day to 60 on the day he was discharged. The temperature ranged from 99.4 after the mercurochrome-220 was given to 96 the day he left the hospital.

Dr. Vischer concluded that the very prompt improvement in these two cases of epidemic encephalitis warrants more extensive trial of mercurochrome-220 in the treatment of such cases. The dosage used was less than that recommended by us.

We are permitted to mention a case recently seen by Dr. L. F. Barker, Baltimore, in consultation with Dr. E. W. Bitzer of Tampa, Fla.

The case was one of lethargic encephalitis in a young woman. The patient was in a state of marked lethargy with inability to move the limbs or speak or take food by herself. The whole picture was characteristic of lethargic encephalitis in Dr. Barker's opinion.

It was decided to give mercurochrome-220 intravenously. Three daily doses of 10 c.c. of a 1 per cent. solution of mercurochrome-220 were given, and they were followed by very quick improvement in muscle movement and in speech. The patient went on to a rapid convalescence.

SIX CASES OF MENINGITIS

Cases 198 and 199 (Schwartz[114]).—Schwartz used mercurochrome-220 in two cases of brain and meningeal infection, which were the result of mastoids, with very interesting results. Both patients responded remarkably, and went on to a rapid cure. In one case, the spinal fluid was changed from cloudy with 1,500 cells to clear with 6 cells.

Case 200 (Tyler[115]).—The patient had meningitis following otitis media. A lumbar puncture was made. Cultures yielded a streptococcus that was neither hemolyticus nor viridans. Two intravenous doses of 30 c.c. of 2 per cent. mercurochrome-220 were given intravenously. There was practically no effect on the spinal fluid or the leukocyte count. The patient died.

Case 201 (Berghausen[116]).—The patient had meningitis following measles. The spinal fluid revealed pus cells and diplococci (streptococcus-pneumococcus group). A culture yielded the same organisms in large number. An intravenous injection of 5 c.c. of 2 per cent. mercurochrome-220 was given. No reaction followed. The patient died several days later.

Case 202 (Schwartz[114]).—The patient had a brain abscess. An intravenous injection of mercurochrome-220 (dose not stated) was given. Death followed forty-eight hours later. Necropsy showed evidence of dye in every organ of the body. This was a very desperate case and for a time it had looked as if the drug would stem the infection.

Case 203 (Adams,[36] Case 4).—A girl, aged 11 years, had meningitis. The spinal fluid showed pneumococcus. The patient received local treatment in the spinal canal with 0.5 per cent. mercurochrome-220 and 20 c.c. of 1 per cent. solution intravenously. No reaction followed. Death occurred two days later.

ONE CASE OF ROCKY MOUNTAIN SPOTTED FEVER

Case 204 (Greeley[117]).—*Rocky Mountain spotted fever. Intravenous injection of 20 c.c. of 1 per cent. mercurochrome-220. Recovery.*

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114. Personal communication from Dr. A. H. Schwartz, Duluth, Minn.

115. Personal communication from Dr. G. T. Tyler, Greenville, S. C.

116. Personal communication from Dr. B. Berghausen, Cincinnati.

117. Greeley, H. P.: Mercurochrome-220 Soluble in Rocky Mountain Spotted Fever, J. A. M. A. **83**:1506 (Nov. 8) 1924. Greeley says: "I am reporting this case of disease which has never responded to any method of treatment, but treatment given was apparently of value."

A woman, aged 28, was admitted to the Madison General Hospital, May 5, 1924. Sixteen days before, she had been bitten by a tick while in southeastern Montana. Eleven days later, while on a train coming east, she had a chill followed by vomiting and fever, ranging between 102 and 104. She had suffered constantly from a splitting headache and acute generalized pains in the muscles, accompanied by exquisite tenderness. The stools for some days before entrance were tarry. Soon after the onset, generalized spotted rash appeared. She was quarantined for smallpox but released by Dr. Vogel, who made a diagnosis of spotted fever.

The patient, who was short and stout, was acutely ill, highly flushed, in severe pain, and not able to move. The skin was covered throughout with a maculopapular rash, in size from a pinhead to a split pea, some spots being erythematous but the most of them hemorrhagic. The thighs and arms were more affected than the body. The face was relatively free. The same rash appeared in the mouth, with submucous hemorrhages in the soft palate. The tonsils had been removed, and there was no general throat infection. The

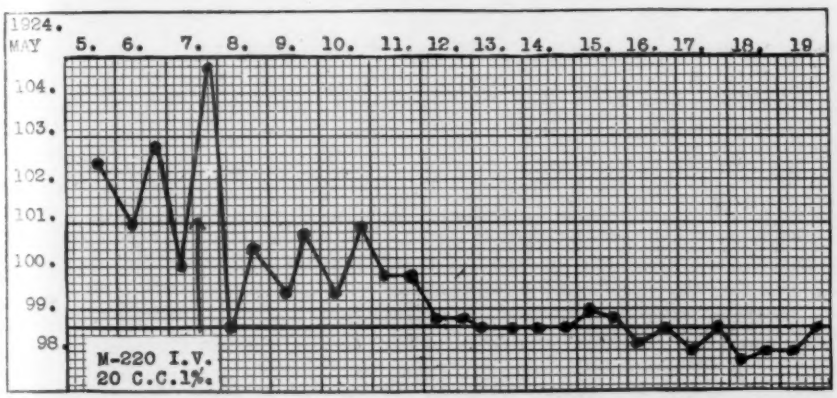

Fig. 15 (Case 204).—Temperature before and after intravenous injection of 20 c.c. of 1 per cent. solution of mercurochrome-220 soluble in case of Rocky Mountain spotted fever.

lymph nodes were slightly enlarged in the neck, axillae and groins. There were numerous coarse râles in the lungs. The heart was negative. The abdomen was not distended, and no spasm was present. There was slight generalized tenderness, and no masses. The deep reflexes were normal. No Kernig's sign was present. A nearly healed spot or tick bite presented itself at the crest of the ilium on the right side. The white blood cells totaled 12,400; the red blood cells, 4,500,000. No malarial organisms were found. Urinalysis was negative. The temperature ranged between 100 and 102.8. The diagnosis of spotted fever was confirmed.

May 7, an intravenous injection of 20 c.c. of 1 per cent. mercurochrome-220 was given. Within an hour there was a severe chill, and the temperature rose to 104.8. Within six hours, the muscular pains and soreness began to leave and, after twelve hours, were entirely gone except in the neck and head. There were intestinal cramps, which were not severe, some diarrhea and salivation. The temperature fell to normal the next morning, but rose each night for two more days to 100.8. It then fell to normal and stayed there. The whole febrile

period was nine days (Fig. 15). Clinically, the disease was arrested by the mercurochrome-220, with the exception of the headache and painful neck, which continued for five days.

Dr. Greeley hoped that his experience might lead physicians in the West, where fever is so fatal, to give mercurochrome-220 further trial.

ONE CASE OF BUBONIC PLAGUE

The following case is cited with comments from the officers of the U. S. Public Health Service simply to show that mercurochrome-220 may be used without danger in bubonic plague, and possibly with great benefit.

As soon as we saw by the newspapers that plague of the pneumonic type had entered the United States, we suggested the use of mercurochrome-220 in these cases to officers of the U. S. Public Health Service. Cooperation was shown by this service. We herewith give an abstract of an interesting case in which Rucker independently gave mercurochrome-220 to a patient with bubonic plague.

CASE 205 (Rucker[118]).—J. V. S., a man, aged 25, was admitted, Oct. 28, 1924. The patient was very ill. The temperature was 40.4 C. (105 F.), pulse 108, and respiration 36. The chest, heart and abdomen were negative. The skin, genito-urinary and rectal examinations were negative. The white blood cells totaled 17,200. The specific gravity of the urine was 1.020. There was no albumin, few casts and no pus. The feces and Wassermann reactions were negative. He stated that he had had a small blister on the left ankle, October 19, and that the glands of the left femoral region began to swell. October 26, he had been quite ill, with swelling in the left groin. Examination showed a phlyctenule on the left ankle which was dried up. In the left groin, there was a large mass of indurated glands, 2½ inches (6.2 cm.) in greatest breadth. No other glands were palpable.

October 29, the patient continued to be very ill. The morning temperature was 105. At 6:30 p. m., an intravenous injection of 30 c.c. of 1 per cent. mercurochrome-220, 4.1 mg. per kilogram, was given. Blood cultures taken just before the administration of the mercurochrome-220 showed, twenty-four hours later, small bipolar rod shaped organisms, gram-positive, which seemed like *Bacillus pestis*. These colonies were afterwards inoculated into animals, and positive diagnosis of bubonic plague was made. The temperature did not rise after the intravenous injection of mercurochrome-220 but fell twenty-four hours later to 101.5. October 31, at 9 a. m., an intravenous injection of 30 c.c. of 1 per cent. mercurochrome-220, 4.1 mg. per kilogram, was given. No reaction followed. The temperature dropped to 100.5 twelve hours later. After this the temperature never arose above 103, but the patient continued to have an up and down slight fever for a time thereafter. In the evening of October 31, the patient developed respiratory symptoms, and in the expectoration *B. pestis* was found. November 1, a small area of consolidation, smaller than usually found in bronchopneumonia, was present in the right lung. The diagnosis was subacute bronchopneumonia. The morning of November 1, a femoral gland was punctured and a stained

118. Personal communication from Dr. W. W. C. Rucker, U. S. Marine Hospital, No. 14, New Orleans.

smear of the secretion showed typical bipolar organisms. At 2 p. m., 140 c.c. of plague serum ten years old was administered. There was a slight reaction of less than 1 degree. November 2, 80 c.c. of plague serum was given. The progress of the case did not seem to be modified by the injection of the plague serum, but went on to a slow but satisfactory convalescence.

To what extent mercurochrome-220 entered into the cure of this patient cannot be stated. It was the opinion of the staff that mercurochrome-220 tided the patient through the critical period, and it was believed that had a third dose of mercurochrome-220 been given immediately, visible results would have been obtained. Of course, this will always remain a question, Dr. Rucker said.

He also stated that plague serum has one disadvantage in the treatment of plague in that it causes an initial reaction that sometimes proves fatal. It is believed that mercurochrome-220 has its value in the treatment of plague and should by all means be used, especially in the absence of plague serum, in that no reaction after injection occurs. This case was unusual in that it showed all three types of plague. Of course, one case is not sufficient evidence on which to base any definite conclusion, but Dr. Rucker felt that the results obtained in this instance were sufficiently encouraging to warrant the use of the drug in subsequent cases. The patient is on the highroad to recovery. The bulk of the bubo resolved without suppuration. One small pocket of pus was drained.

McCoy,[119] Director of the Hygienic Laboratory, U. S. Public Health Service, says, "Antiplague serum is of so little worth and so uncertain in its action that I believe that mercurochrome-220 had more influence in this case than the serum."

FOURTEEN CASES OF PLAGUE TREATED IN LOS ANGELES GENERAL HOSPITAL WITH MERCUROCHROME-220

A letter from Assistant Surgeon-General W. F. Draper, U. S. Public Health Service, gives the following abstracts of cases treated by Dr. E. S. Safarik:

October 31, the day that the organism was first found, a nurse who had been caring for the first victim during his few hours in the pneumonia ward the previous week was admitted to the hospital suffering with a severe pain in the chest and back and a fever which she said had been coming on for two days. Soon she developed difficulty in breathing; she coughed and expectorated, and on the following morning the expectoration was blood stained. A large, painful swelling appeared in the glands of the neck. As a desperate resort she was given 30 c.c. of 1 per cent. solution of mercurochrome-220 intravenously and during the week received several additional injections. There was a noticeable improvement in her condition, and she appears at the present time to be proceeding toward convalescence. As yet, however, no bacteriologic confirmation has been secured in this case.

In another case, clinically diagnosed pneumonic plague, the patient got well after several mercurochrome-220 injections of 5 mg. per kilogram. In eleven cases of pneumonic and one of bubonic plague, the patients died, but in all but

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119. Personal communication from Dr. G. W. McCoy, Washington, D. C.

one only one injection of mercurochrome-220 was employed. In several there was definite clinical improvement with temperature drops and the duration of life was lengthened; one patient lived thirteen days.

These cases are, of course, much too incomplete to furnish a basis for conclusions, but owing to the malignant nature of the disease and its high mortality, the mere fact that mercurochrome-220 has been used with benefit is, we believe, of interest.

ONE CASE OF SCARLET FEVER

CASE 206 (Young and Birkhaug[4]).—*Scarlet fever. Pharyngitis. Tonsillitis. Adenitis of neck. Erysipelas. Septicemia. Intravenous injection of mercurochrome-220, 7.5 mg. per kilogram. Rapid recovery.*

A boy, aged 4 years, was admitted, March 2, 1924, with flushed cheeks, discharging nose, sordes on lips, the entire faucial ring deeply strawberry red and both tonsils slightly enlarged, cryptic and slightly exudative. The temperature was 103.2, pulse 134 and respiration 28. A diagnosis of scarlet fever was made. March 4, the condition grew worse. There was evidence of erysipelas on the face. The temperature was 104.4. March 5, the patient was steadily growing worse. The toxic condition was aggravated. The spleen was large. The white blood cells totaled 30,600. At 10:30 p. m., after a preliminary sensitization test had proved negative, 40 c.c. of Dochez' antistreptococcic serum was injected intramuscularly in the right buttock.

March 6, at 9 a. m., the temperature fell from 104 to 101, but the toxic symptoms were just as marked as before the serum. The erythema on the face had continued to spread. The cervical glands were greatly enlarged. A blood culture was made, which was reported *Streptococcus hemolyticus,* thirty-eight colonies per cubic centimeter. March 7, the patient was drowsy and delirious. The infection of the skin had extended. The urine showed albumin, white blood cells and granular casts. Blood examination showed the leukocytes to total 32,780. March 8, the temperature was 105, pulse 140 and respiration 37. No improvement was noted. The erysipelas was spreading. The glands of the jaw were greatly enlarged. A blood culture yielded *Streptococcus hemolyticus.* The white blood cells totaled 36,960.

As the patient was steadily growing worse, the condition was desperate. As the injection of serum three days before had not arrested the progress of the disease, it was decided to give an intravenous injection of mercurochrome-220. March 8, at 9 p. m., 15 c.c. of 1 per cent. solution, 7.5 mg. per kilogram, was given. No marked reaction was noted. The next morning, the condition was markedly improved. The patient was less toxic and had no delirium.

A blood culture twelve hours after the intravenous injection of mercurochrome-220 was sterile and subsequently the temperature fell from 105 to 101, the pulse from 140 to 98. Leukocytes totaled 15,200. March 10, there was rapid and continuous improvement. A blood culture was sterile. March 11, the temperature was 99.8, pulse 88 and respiration 28. The throat was almost normal. The cervical glands were hardly palpable. Leukocytes total 9,160. March 12, there was continued progress. Urinalysis showed no albumin and no casts. The urine was sterile. The condition was excellent. March 16, there was continued improvement. The patient apparently was well. The urine was normal. The patient was discharged.

THREE CASES OF TUBERCULOSIS

CASE 207 (Wolff [107]).—A colored girl, apparently dying of lung tuberculosis and in a moribund state, was given an intravenous injection of 10 c.c. of 1 per cent. mercurochrome-220. The temperature dropped from 103 to 101. The patient lived for ten days. This case was encouraging in that the injection caused no ill effect and had a beneficial effect temporarily.

CASE 208 (Wolff).—A woman, aged 54, had an extensive involvement of both lungs and large cavities. The life expectancy was probably two weeks. She had a high fever, 103, daily. An intravenous injection of 1 per cent. mercurochrome-220 was given once weekly, 7 c.c., 10 c.c. and later 15 c.c. After the 15 c.c. dose the temperature was 103. The patient had mild stomatitis, but no diarrhea. The patient began to improve immediately after the second injection of 10 c.c. In a month, she was out of bed. The daily temperature fell to 99; the cough and expectoration diminished greatly and the patient lived for three months, apparently improved and in good condition. She died suddenly. Necropsy showed a dilated heart. The lung cavities were lined with clean red granulation tissue, and there was almost no pus or mucus on macroscopic examination. Other physicians also confirmed the remarkable absence of pus and caseation. This is an example of an extremely advanced case that was greatly improved by intravenous injection of mercurochrome-220.

CASE 209 (Wolff [112]).—In another case of lung tuberculosis, Dr. Wolff used mercurochrome-220 to kill the secondary infection. The patient, a woman, is now free from fever and coughing, and spits very little. Tubercle bacilli are still present, but she seems on the road to recovery. It is now eight months since treatment began and she has gained 13 pounds (5.9 kg.). Dr. Wolff was sure that without mercurochrome-220 to kill the secondary infection this woman would have died.

Clinical data on hand are much too brief to draw any deductions on the use of mercurochrome-220 in tuberculosis of the lungs. As secondary invasion by pyogenic organisms has been shown to be responsible for many of the "septic" symptoms and consequent rapid weakening of the patient, mercurochrome may well prove of great value to combat such septic conditions, if not the tuberculous process itself.

FOUR CASES OF PERITONITIS [120]

We have very brief reports that seem to indicate that mercurochrome-220 may be of some use in cases of postoperative peritonitis. These cases are interesting, but too few to draw deductions from.

CASE 210 (Roeder and Judd [81]).—*Peritonitis following operation for appendiceal abscess. Intravenous injection of 30 c.c. of 1 per cent. mercurochrome-220. Recovery.*

A white man, aged 41, following drainage of a retrocecal appendiceal abscess, had advanced peritonitis. The pulse rose steadily to 130; the temperature was 102. An intravenous injection of 30 c.c. of mercurochrome-220 was followed by a temperature of 104, with diarrhea in forty-eight hours. The temperature

120. Reference should also be made to Cases 29 and 78.

went down to 99, the pulse to 80 in a few hours. The change was so striking that Roeder and Judd say that mercurochrome-220 was the deciding factor.

In another case, mercurochrome-220 failed to save a patient with peritonitis following colectomy.

CASE 211 (Hopkins[73]).—A boy, aged 12, weighing 75 pounds (34 kg.), had a gangrenous appendix removed. A peritoneal abscess was drained. An intravenous injection of 30 c.c. of 0.5 per cent. mercurochrome-220 was given. Another abscess was drained. The patient was discharged well. The mercurochrome injection was followed only by a drop in temperature. The benefit was doubtful.

CASE 212 (Hopkins[73]).—A woman, aged 27, had general peritonitis. She was in a moribund condition. An intravenous injection of 30 c.c. of 1 per cent. mercurochrome-220 was given. No reaction followed. The patient died nine hours after admission.

CASE 213 (Roeder and Judd[21]).—A patient had peritonitis following excision of the colon. The temperature was 105. The white blood cells totaled 4,000. There was a definite picture of peritonitis. An intravenous injection of 30 c.c. of 1 per cent. mercurochrome-220 was given. Twenty-four hours later, a second injection was given. Marked weakness and shock continued. The patient died in twenty-four hours.

DOSAGE AND REACTIONS

Cases Treated in Brady Urological Institute.—In Table 12, eighteen patients were given 5 mg. per kilogram. There are five cases in this group that show marked temperature, chill and gastro-intestinal reactions. Of this number, three of the patients were very fat, weighing 77, 80 and 89 kg. They therefore received large amounts of the drug (38.5, 40 and 44.5 c.c. of a 1 per cent. solution).

Two patients had moderate gastro-intestinal reactions with marked temperature and chill reactions.

One patient had a marked gastro-intestinal reaction and moderate temperature and chill reactions.

Eleven patients in this group had moderate or slight reactions.

Only five patients had stomatitis, and one of these but slightly. In three other cases, it did not occur until two or more injections had been given. In none of these cases did the teeth become more than slightly loose.

Five patients had casts in the urine soon after treatment, but in all except one, who had an occasional cast when discharged ten days after the last treatment, the presence of casts was quite temporary. All were free from them on discharge. One patient having *Streptococcus viridans* endocarditis, with septicemia and foci of infection in the kidneys, had a constantly increasing number of casts in the urine until death. In this instance, the findings could not be blamed entirely on the drug employed. One patient having occasional casts in the urine on admission left the hospital after treatment with the urine unchanged.

Four patients showed a temporary increase in the red blood cells in the urine after treatment.

Six patients were given 3 mg. per kilogram. One patient had a very marked reaction, but was practically moribund at the time of treatment.

Another patient who had a marked reaction was very ill from generalized tuberculosis at the time of injection.

The four remaining cases showed only slight reactions.

There was no stomatitis in this group.

In two cases, there was no record of the urine at the time of discharge. In the four remaining cases, there were no casts present in the urine at discharge.

One patient was given 8.2 mg. per kilogram. This patient was only 4 years of age, and weighed only 12 kilograms. Injection was followed by a marked drop in temperature. There was no gastro-intestinal reaction. She subsequently received 2.5 mg. per kilogram on four consecutive days with no reaction. At no time during treatment did casts appear in the urine.

One patient was given 6.8 mg. per kilogram. This patient had a very marked gastro-intestinal and a marked temperature and chill reaction. In view of the man's age, 68 years, and his weight, 82 kilograms, the reaction was no more severe than one would expect after such dosage. Soon after treatment, there were a few casts and a few red blood cells in the urine, but these disappeared in a few days.

One patient was given 2.5 mg. per kilogram. In this case, there was only a slight increase in temperature and slight nausea.

Outside Cases.—Reactions have been analyzed in seventy case reports from elsewhere, in cases that offered enough detail to make this possible. From this study, the following observations have been made.

Chill.—Of these seventy cases, in thirty-one, or 44.2 per cent. of this series, rigor was mentioned as having been present after the intravenous injection of mercurochrome-220. The chill was slight after three injections, marked after ten, and not qualified in twenty cases.

The slight chills came after injections of 5.9 mg. per kilogram (second injection), and after 25 and 30 c.c. of 1 per cent. solution. The marked chills came after doses of from 2.2 to 5 mg. per kilogram in the six instances in which the exact dose could be determined. In one case, the chill was severe after an initial dose of 4.7 mg. per kilogram, but slight after a second injection of 5.9 mg. per kilogram.

The duration of the chill was specified seven times. The minimum was six minutes and the maximum three hours following an initial injection of 5 mg. per kilogram.

TABLE 12.—*Reactions in Twenty-Seven Cases After Administration of 5 Mg. Per Kilogram of Mercurochrome-220 Soluble*

Dosage	Initials, Age, Weight	General Condition Before Drug	Diagnosis	Treatment	Temperature and Chill Reaction	Gastrointestinal Reaction	Stomatitis	Condition of Urine: Before Infection	Condition of Urine: After Infection	Condition of Urine: Ultimately	Result	Remarks
M-220 I.V. 5 mg. per kg. 18 cases	H. A. S. 64 yr. 80 kg.	Fair	Furunculosis	1 dose mercurochrome-220	Marked	Marked	Marked	Albumin +++ Pus ++++	Albumin ++ Pus +++ R.B.C. few	Albumin + Pus +	Cured	Cultures from arm: Staphylococcus aureus
	D. J. C. 64 yr. 65 kg.	Bad	Staphylococcic septicemia	1 dose mercurochrome-220	Moderate	Moderate	None	Albumin +++ Pus +++ R.B.C. ++	Albumin ++ Pus +++ R.B.C. ++++	Negative findings	Failed	Blood cultures: Staphylococcus albus. Gentian violet also failed. Cleared following a transfusion of 500 c.c. of citrated blood
	R. M. 63 yr. 56 kg.	Very bad	Pyonephrosis	1 dose mercurochrome-220 1 dose gentian violet, 5 mg. per kg.	Marked	Marked	None	Albumin + Pus ++	Albumin + Pus ++ R.B.C. +	Albumin + Pus +	Greatly improved	Cultures became free from gram-negative bacilli for a few days
	J. M. J. 56 yr. 66 kg.	Bad	Streptothrix of lung	2 doses mercurochrome-220	T. increase no chill	Moderate	None	Albumin + Pus + R.B.C. +	Albumin ++ Pus + R.B.C. +	Same as before treatment	Improved	Streptothrix actually isolated
	J. T. 50 yr. 68 kg.	Very bad	Seminal vesicular abscess, tuberculosis on microscopic study	1 dose mercurochrome-220	No chill	Moderate	Slight	Albumin ++ W.B.C. few Occasional casts	No record	No record	Failed	Cultures: Prostatic fluid, colon bacilli and cocci. Cultures from urine: Colon and cocci
	M. A. 58 yr. 77 kg.	Good	Bacilluria	1 dose mercurochrome-220	Marked	Marked	None	Albumin + W.B.C. few Occasional casts	Albumin + W.B.C. few R.B.C. few Few casts	Same as before treatment	Failed	Cultures: Colon group bacillus
	I. G. 49 yr. 80 kg.	Fair	Chronic bilateral pyelitis	1 dose mercurochrome-220	No reaction	Marked	None	Albumin + W.B.C. ++ R.B.C. +	Albumin ++ W.B.C. +++ R.B.C. ++ Many casts	Albumin + No casts	Cured	Cultures: Gram-negative bacillus
	G. A. W. 47 yr. 58 kg.	Bad	Chronic prostatitis, arthritis	2 doses mercurochrome-220	Moderate	Moderate	None	W.B.C. few	No change	Occasional W.B.C.	Cured	Cultures of urine and prostatic secretion; Staphylococcus albus
	H. A. D. 44 yr. 68 kg.	Very bad	Colon septicemia	1 dose mercurochrome-220	Marked	Moderate	None	Albumin + Pus ++++	Not recorded	Albumin + Pus + No casts	Cured	Blood cultures: Colon group bacillus
	B. B. 38 yr. 75 kg.	Bad	Periurethral abscess	1 dose mercurochrome-220	None	Marked	None	Albumin trace Pus +	Not recorded (could not void)	No albumin No casts Pus +	Failed	Cultures: B. proteus and streptococcus
	G. C. D. 37 yr. 65 kg.	Fair	Left pyelitis	2 doses mercurochrome-220 (3 mg. per kg.; 5 mg. per kg.)	Moderate	Moderate	None	Albumin trace Pus +	No change	No change	Failed	Cultures: Bacillus paratyphoid group
	S. H. C. 36 yr. 89 kg.	Good	Pansinusitis	2 doses mercurochrome-220 1 dose gentian violet, 5 mg. per kg.	Marked	Marked	None	Negative findings	Albumin + W.B.C. few Casts few	Discharged 2 days after treatment	Failed	Cultures: Pneumococcus Group IV
	G. R. 29 yr. 57 kg.	Bad	Streptococcus viridans, endocarditis and septicemia	2 doses mercurochrome-220	Temp. increase	Slight	Marked after second injection	Albumin ++ No casts No R.B.C. No W.B.C.	After 2d injection alb. ++ No casts Few R. B. C. Few W.B.C.	No change	Failed	Blood cultures: Streptococcus viridans, 150 to 300 per cubic centimeter

	B. B. 28 yr. 60 kg.	Fair	Ulcerative balanoposthitis	3 doses mercurochrome-220	Moderate	Moderate	Marked after second injection	Few W.B.C.	Many W.B.C. Few R.B.C. Albumin + Many casts	Same as before treatment	Cured	Cultures: Streptococci, staphylococci and bacilli
	C. B. T. 27 yr. 58 kg.	Bad	Streptococcus viridans, endocarditis and septicemia	3 doses mercurochrome-220 5 mg. per kg.; 1 dose mercurochrome-220, 8 mg per kg. plus other intravenous therapy	Temp. increase	None	Marked after fourth injection	Pus + Few granular casts	Many granular casts Albumin ++ Pus +	Many casts Albumin +++ Pus +	Failed	Blood cultures: Streptococcus viridans, 180 per c.c. Patient received 1 dose, 8 mg. per kilogram
	F. P. 26 yr. 80 kg.	Bad	Gonorrheal arthritis and prostatitis	2 doses mercurochrome-220	Marked	Moderate	None	Many W.B.C.	Albumin + Many W.B.C. Few R.B.C. Few casts	Albumin trace Occasional cast and R.B.C. Few W.B.C.	Greatly improved	Slides and smears showed gonococci
	W. A. 22 yr. 66 kg.	Fair	Perirenal abscess, urinary infection	2 doses mercurochrome-220; 1 dose gentian violet, 5 mg. per kg.	Moderate	Marked	None	Albumin ++ Pus +	Albumin + Pus + Occasional cast	Negative findings	Improved	Culture, perirenal puncture: staphylococcus. Culture of urine: Staphylococcus aureus
	J. H. D. 17 yr. 55 kg.	Bad	Perirenal abscess	1 dose mercurochrome 220	Very marked	None	None	Albumin + Pus, few cells	No report	Few W.B.C. Few R.B.C.	Cured	5.4 mg. per kilogram. Clinical case. No cultures obtained
M-220 I.V. 6.8 mg. per kg.	H. P. 68 yr. 82 kg.	Good	Chronic prostatitis and bacilluria	1 dose mercurochrome-220	Marked	Very marked	None	Albumin + Few W.B.C. No casts	Albumin + Few W.B.C. Few granular casts	Same as before treatment	Symptomatically better; improved	Cultures of urine and prostatic secretion always positive
M-220 I.V. 8.2 mg. per kg.	M. L. 4 yr. 12 kg.	Very bad	Pyelitis	1 dose mercurochrome-220, 8.2 mg. per kg.; 4 doses mercurochrome-220 2.5 mg. per kg. each	Marked drop in temp., no chill	None	None	Albumin ++++ Pus ++++ B. coli ++++	Albumin +++ Pus +++ B. coli +++	Albumin + Pus + B. coli +	Life saved; urinary infection; improved	Cultures: B. coli. Intravenous injection of mercurochrome-220, 2.5 mg. per kilogram four consecutive days with no reaction
M-220 I.V. 3 mg. per kg. 6 cases	C. V. H. 69 yr. 60 kg.	Fair	Peridental abscess	1 dose mercurochrome-220	Slight	Slight	None	Pus ++ Albumin +	No record	Pus, few cells Albumin, trace	Failed	Cultures not taken
	E. R. M. 68 yr. ? kg.	Good	Chronic prostatitis	3 doses mercurochrome-220	Slight	Moderate	None	No albumin, casts or R.B.C. Few W.B.C.	No record	No record	Failed	Urine smear: Cocci
	J. M. B. 60 yr. 68 kg.	Good	Chronic cystitis	1 dose mercurochrome-220	None	None	None	Albumin, trace Few W.B.C.	No record	Not obtained	Cured	Culture: Gram-positive cocci; negative after second hour
	H. A. B. 29 yr. 50 kg.	Very bad	Generalized tuberculosis	1 dose mercurochrome-220	Marked	Marked	None	Pus ++ Few R.B.C.	Pus ++ Albumin + R.B.C. few	Casts never found	Failed	Tuberculosis bacilli found in scrotal wound
	W. S. 24 yr. 53 kg.	Practically moribund	Generalized tuberculosis	1 dose mercurochrome-220	Very marked	Very marked	None	Normal	Patient incontinent of urine	.....	Failed	Patient died 36 hours after injection; general tuberculosis found at necropsy
	M. G. 18 yr. 54 kg.	Bad	Pyonephrosis	1 dose mercurochrome-220	Temp. up 1 degree	None	None	Albumin, trace Many W.B.C. Few R.B.C. No casts	Albumin + Many W.B.C. Few R.B.C. No casts	Same as before treatment	Failed	Cultures: Staphylococci
M-200 I.V. 2.5 mg. per kg.	J. E. 26 yr. 52 kg.	Very bad	Ureteral calculus and pyelitis	2 doses mercurochrome-220, 2.5 mg. per kg.	Temp. up 1 degree	Slight	None	Albumin ++ Inf. ++ Pus + R.B.C. +++	No change	No change	Failed	Two injections of 2.5 mg. per kilogram two hours apart. Cultures: Streptococci

Total number of cases, twenty-seven. Of these treatment failed in fourteen cases, among which three had generalized tuberculosis; two Streptococcus viridans endocarditis; and one streptothrix pneumonia. Eliminating these six hopeless cases, there remain twenty-one cases. Of these there were cured, seven (33 per cent.); greatly improved, three (14 per cent.); improved, three (14 per cent.), and failed, eight (38 per cent.).

Temperature.—In 50 per cent., or thirty-five of the seventy cases, enough details of temperature changes are given for analysis. These represent thirty-eight injections.

After twenty-two injections, there was first an increase and then a decrease of temperature. The average increase was 2.5 degrees, the minimum 0.2 degrees, the maximum 5.4 degrees. The average decrease after this increase was 6.1, the minimum 4, and the maximum 10 degrees.

After sixteen injections, there was a drop of temperature without any indicated increase. The average drop in this group was 4.6, the minimum 0.4, and the maximum 7 degrees.

In addition to the temperature changes noted, in twenty-two cases not included in the series of seventy, the only reaction noted was a drop in temperature to normal or near normal.

Diarrhea, Nausea and Vomiting.—Of this series of seventy cases, 40 per cent., or twenty-eight patients, had diarrhea. Of these six were described as marked, five as moderate and one as slight. Eighteen were not qualified.

Of the six marked diarrheas, two showed blood and mucus, one after only 10 c.c. of 1 per cent. solution, one after 5 mg. per kilogram. The other severe diarrheas followed doses of from 1.1 to 5 mg. per kilogram.

However, the moderate diarrheas followed doses of from 1.5 to 5 mg. per kilogram, so that it is impossible to decide from these cases that the severity of the diarrhea is in proportion to the dose. The evidence seems to indicate that it is not. It is more probably due to individual variations in the patients.

Nausea without vomiting is recorded in four cases, 5.7 per cent. of the series of seventy.

Vomiting is reported in twenty cases, or 28.5 per cent. of the series of seventy.

The nausea and vomiting are of course closely parallel to the diarrhea.

Abdominal pains are noted in seven cases, 10 per cent. of the series, intense in three cases, unqualified in four cases.

Stomatitis.—Fifteen patients, or 21.4 per cent. of the seventy cases in this series, who received a total of fifty-two injections, developed stomatitis. These cases are analyzed in Table 13, which may be summarized as follows:

1. In only one case did salivation occur after a single dose (20 c.c. of 1 per cent. solution).

2. In the five cases receiving two injections which developed stomatitis, two showed only salivation, one showed salivation and soreness of the gums, and two soreness of the gums.

3. The patients receiving three or more injections and developing stomatitis received intensive treatment; in some of these cases daily injections were given.

It may be concluded that usually stomatitis occurs only after repeated injections.

In every case of which we have records, the stomatitis disappeared within a few days. It rarely lasted longer than a week.

Cases Showing No Reactions.—In addition to the seventy in this series, totaling eighty-nine injections, in six cases it was definitely stated that there was no reaction. Yet only one of these patients, who

TABLE 13.—*Stomatitis in Cases from Outside Brady Urological Institute*

No. of Injections	Dose	Reaction	No. of Cases	Percentage of Stomatitis Cases	Percentage of Reaction Series (70)
1	20 c.c. 1%	Salivation only	1	6.6	1.4
2	(1) 15 c.c. of 1% solution 24 hours after first dose of 20 c.c. of 1% solution	Salivation only	5	33.3	7.1
	(2) 2.9 mg. per kilogram 24 hours apart	Salivation only			
	(3) 2 doses of 25 c.c. 1% solution	Salivation and sore gums			
	(4) 2 doses of 4.1 mg. per kilogram 13 days apart	Sore gums after second dose			
	(5) 2 doses of 4.7 mg. per kilogram 2 days apart	Sore gums			
3	(1) 3 doses of from 2 to 4 mg. per kilogram daily	Stomatitis	2	13.3	2.8
	(2) 3 doses totaling 7 mg. per kilogram	Stomatitis			
4	(1) 4 doses of from 2 to 4 mg. per kilogram daily	Stomatitis	3	20.0	4.2
	(2) 4 doses totaling 10 mg. per kilogram	Stomatitis			
	(3) 4 "graduated doses"	Stomatitis			
5	5 doses of from 2 to 4 mg. per kilogram daily	Stomatitis	1	6.6	1.4
6	(1) 6 doses of from 3.4 to 5 mg. per kilogram	.....	3	20.0	4.2
	(2) 6 doses of from 10 to 20 c.c. 1% solution	.....			
	(3) 6 doses of from 10 to 25 c.c. 1% solution	.....			
			15	....	21.1

had streptococcus meningitis and who had received 5 c.c. of a 2 per cent. solution, was not benefited by the injections. The other five patients were all markedly improved. Two of these had puerperal sepsis. One of the two had three doses, the first 2.5 grains (0.16 gm.), the second 2.5 grains six hours later, and the third 3 grains (0.19 gm.) twelve hours later. The second of the sepsis patients had one dose of 5 mg. per kilogram, no statement being made as to reaction when the second dose of 5 mg. per kilogram was given. The third case in this group was one of pyelonephritis which was apparently cured by two injections of 3 mg. per kilogram.

The remaining two cases were encephalitis. One of the patients received 1.5 mg. per kilogram, the other 10 c.c. of 1 per cent. solution.

These favorable results without reaction, although limited in number, at least suggest that the theory held by some, that the reaction and the therapeutic action of intravenous injections of mercurochrome-220 are parallel, is not tenable.

The reactions of the cases not from this clinic are summarized in Table 14.

TABLE 14.—*Classification of Reactions in Seventy-Two Cases (Ninety-Three Injections)*

Reaction	Cases		Injections	
	Number	Per Cent.	Number	Per Cent.
None	16	22.1	18	19.4
Slight	22	31.0	33	35.5
Moderate	10	13.9	16	17.2
Marked	21	29.0	23	24.7
Very marked	3	4.0	3	3.2
	72	100	93	100

In forty-eight cases, or 66⅔ per cent., there was no reaction, or it was slight or moderate; it was marked in twenty-one cases, or 29 per cent., while it was very marked in only three cases, or 4 per cent.

An analysis of cases by the organisms causing the infection is given in Table 15.

From this table it will be seen that of the ninety-seven cases seventy-eight, or 80.3 per cent., were cured, sterilized or improved by the use of the drug. The percentage of cures, sterilizations or improvements was greatest in infections due to *B. coli* (81.8 per cent.), staphylococcus (80 per cent.) and the gonococcus (80 per cent.). It was less with gram-positive diplococci, including the pneumococcus (66.6 per cent.) and with *Streptococcus hemolyticus* (53.8 per cent.), and least in *Streptococcus viridans* cases (33.3 per cent.). While the cases are limited in number and possibly represent a higher percentage of good cases than a larger series would show, they may be taken as indicating the action of mercurochrome-220 against the more common organisms found in infection.

Conclusions Regarding Reactions.—By giving small doses of mercurochrome (3 mg. per kilogram), as a rule, practically no reaction is encountered after the first injection, and two or three more can usually be given before the gums become sore and slight stomatitis develops. In rare instances, stomatitis may occur early from a small dosage. When injections of 4 or 5 mg. per kilogram are given, especially in the presence of fever, a marked febrile reaction followed by a marked drop in temperature usually occurs. The most uncomfortable reactions, which often occur with these doses, are nausea and vomiting. These may be very marked and lead to great discomfort and occasionally to dysenteric stools, at frequent intervals, for twenty-four hours. It is

TABLE 15.—*Results in Ninety-Seven Cases Treated with Mercurochrome-220 Intravenously, Classified Bacteriologically*

Organism	Culture	Diagnosis	Totals	Cured or Sterilized	Improved; Recovery	Percentage Cured or Improved	Improved, Later Complications	Effect of Mercurochrome-220 Doubtful	Failed	
									No.	Per Cent.
Streptococcus hemolyticus	Pure	Septicemia	9	3	..	....	1	1	4	....
		Endocarditis	1	1	..	....	..	..	..	....
		Pneumonia	1	1	..	....	..	..	..	....
		Abscess	1	..	1	....	..	..	..	....
	Mixed (Staph.)	Erysipelas and osteomyelitis	1	..	..	....	..	..	..	....
			13	5	2	53.8	1	1	4	30.7
Streptococcus viridans	Pure	Endocarditis	2	..	..	....	..	..	2	....
	Mixed (Staph.)	Endocarditis, etc.	1	..	1	....	..	..	..	....
			3	..	1	33⅓	..	..	2	66⅔
Streptococcus, unclassified	Pure	Septicemia	1	1	..	....	..	..	..	....
		Endocarditis	2	..	..	....	..	..	2	....
		Arthritis	1	1	..	....	..	..	..	....
		Local lesion	2	1	..	....	..	..	1	....
		Meningitis	1	..	..	....	..	..	1	....
	Mixed	Septicemia	5	2	2	....	..	..	1	....
		Pyelonephritis	2	1	1	....	..	..	..	....
			14	6	3	64.3	..	..	5	35.7
Gram-positive diplococci, including pneumococci	Pure	Septicemia	2	2	..	....	..	..	2	....
		Meningitis	2	..	..	....	..	..	..	....
	Mixed	Septicemia	2	2	..	....	..	..	..	....
			6	4	..	66⅔	..	..	2	33⅓
Staphylococci	Pure	Septicemia	9	4	2	....	..	..	2	....
		Endomyocarditis	1	1	..	....	..	..	..	....
		Perinephritic abscess	1	..	1	....	..	..	..	....
		Pyelonephritis	3	2	..	....	..	..	1	....
		Prostatitis	1	1	..	....	..	..	..	....
		Furunculosis	1	1	..	....	..	..	..	....
		Cellulitis	1	..	1	....	..	..	..	....
	Mixed	Septicemia	5	1	3	....	..	..	1	....
		Pyelonephritis	5	3	1	....	..	..	1	....
		Osteomyelitis and erysipelas	1	1	..	....	..	..	..	....
		Gonorrhea	2	2	..	....	..	..	..	....
			30	16	8	80	..	..	5	16
Gonococcus	Pure	Urethritis, acute	4	1	1	....	..	..	2	....
		Urethritis, chronic	9	5	2	....	..	..	2	....
		Prostatic abscess	1	..	1	....	..	..	..	....
		Arthritis	3	2	1	....	..	..	..	....
	Mixed	Septicemia	1	1	..	....	..	..	..	....
		Urethritis, acute	1	1	..	....	..	..	..	....
		Urethritis, chronic	1	1	..	....	..	..	..	....
			20	11	5	80	..	..	4	20
Bacillus coli	Pure	Septicemia	1	1	..	....	..	..	..	....
		Retroperitoneal abscess	1	1	..	....	..	..	..	....
		Pyelonephritis	7	4	2	....	..	..	1	....
		Cystitis and prostatitis	2	1	..	....	..	..	1	....
			11	7	2	81.8	..	..	2	18.2
Total number			97	54	24	....	3	2	30	....
Total percentage			100	55.6	24.7		3.3	2.0	31.9	

interesting to note that, when a second or third injection of equal size is given, the reactions are almost always less and that not infrequently there is no reaction following a dose which produced a very severe reaction at first.

The whole subject of reactions can, therefore, be viewed with little concern. In order to give desperate or very severe cases adequate dosage, it is necessary to inject at least 4 or 5 mg. per kilogram, and in so doing one may expect a certain number of marked reactions. Although producing great discomfort, these are transitory in character and apparently lead to no permanent damage. The severity of the reaction (especially febrile) may even play an important part in the elimination of the infection. They do not cause definite nephritis.

DEATHS FOLLOWING INTRAVENOUS INJECTIONS OF MERCUROCHROME-220

We have received reports of two deaths that we wish to record.

CASE 214 (Gallagher[121]).—A boy, aged 16 years, was admitted, March 22, 1924, with acute and chronic osteomyelitis of the left femur. The white blood cells totaled 20,500. March 27, incision of the left femur was done, and evacuation of a large amount of pus. April 4, a second operation was necessary, and pus was evacuated. April 5, the right and left arms had become edematous; there also was a red area over the sacrum. April 9, multiple incisions were made in the arm, with evacuation of much pus. The temperature continued elevated, from 100 to 102. The pulse was from 120 to 135. Cultures from the pus showed *Streptococcus albus*. A blood culture was negative.

May 12, an intravenous injection of 20 c.c. of 1 per cent. mercurochrome-220 was given. No reaction or untoward symptoms followed. Mercurochrome was again given two days later. When approximately 15 c.c. of a 1 per cent. solution had been slowly injected, the patient suddenly complained of severe pain in the abdomen and a choking sensation over the heart. The entire chest wall could be seen heaving tremendously. A moment later, the heart action ceased. No necropsy was done. The weight was not given; the dosage was probably not over 3 mg. per kilogram.

The second case was reported to me verbally by Dr. Schamberg of Philadelphia.

CASE 215 (Schamberg).—A man, aged 31, weighing 130 pounds (104.3 kg.), had severe pemphigus. He was given an intravenous injection of 32 c.c. of 1 per cent. mercurochrome-220, 5 mg. per kilogram. This was followed by a violent reaction, vomiting, diarrhea, anuria, and the patent died within twenty-two hours. No necropsy was done.

While apparently the drug hastened or brought on the fatal termination in both these cases, it is nevertheless true that both patients were suffering from probably fatal infections. The death of the boy is more

121. Personal communication from Dr. T. G. Gallagher, Schofield Building, Cleveland, Ohio.

remarkable in that, two days before, the same dose caused no reaction. It is possible that he died of embolism and not from the effects of the mercurochrome-220.

COMMENT ON CASES PRESENTED IN THIS PAPER

As we remarked in the beginning, in the compilation of these reports from our own clinic and from others, and in abstracting them for presentation here, we have tried to be conservative in interpretation and in statement. Nevertheless in some instances we, as well as others, have possibly been overenthusiastic. We have endeavored to get a record of all cases, good or bad, and have succeeded, we believe, very well; but we confess that we have probably received a greater proportion of the favorable results and have failed to get some of the negative results. As a whole, the reporters have been remarkably frank in sending cases, good and bad, and we have encouraged them to express themselves critically and freely, and have quoted their comments.

In many cases, details that would give a better picture of the case were missing, and in a few cases the clinical notes that have been furnished us are meager. In our abstracts this is often evident, but in some cases reported here fairly complete notes were given us. It is necessary in conserving space to omit much that might have been interesting. The essentials, however, have usually been given and nearly all the important cases necessary to a demonstration of the value of the drug have been given in fairly complete detail. In cases in which the drug was admitted a failure, it required very few words to make that clear, and the cases have been reported very briefly.

The difficult problem is to prove the value of the drug, and more complete notes are necessary for this demonstration. In arriving at a correct estimation of any form of therapy, great difficulties are always encountered. Such has been the case here, but we have endeavored by diverse classification, studying groups, and making numerous tabulations, to present the facts so that the reader may form his own conclusions from the details at hand. Some of the cases are therefore to be given greater value in this study of evidence than others. Inspection will at once reveal those in which the weight of evidence is present. In therapeutics it is so easy to confound propter hoc with post hoc and also so easy in the enthusiasm of a new idea to view facts in a biased way that the exact truth is difficult to get. Realizing these things, we have endeavored to be on the safe side but, as stated before, we have plainly stated and tabulated the facts. Those who are interested will find considerable material for study and independent judgment.

Technic.—We have recommended (and it has usually been followed) the injection of a 1 per cent. solution made up with freshly distilled water

from the granular form of mercurochrome-220 soluble. Warm water may be used in making this solution, but it should not be boiled as disintegration may occur if the fluid is superheated. In the adult, the injection is made, as a rule, in one of the veins at the bend of the elbow, but other veins may be employed. In children and patients with very small veins, the external jugular or veins of the thighs may be employed, and in infants the peritoneal cavity may be used. We have never seen evidences of irritation of the vein or thrombosis in any of our cases in which mercurochrome was given. In the case of gentian violet, which in a 1 per cent. solution is extremely thick, 0.5 per cent. or 0.25 per cent. solution is preferable.

In our early papers, we advised the full therapeutic dose, 5 mg. per kilogram (22.7 c.c. of a 1 per cent. solution per hundred pounds [45.4 kg.] of body weight), and in the majority of cases here recorded this dosage has been used. In a few instances it has been exceeded, 7 and even 8 mg. per kilogram in succession having been employed. In some instances the dose has been much smaller, and we believe that many of the negative results herein recorded are directly due to the small dosage and the consequent inefficient treatment employed. We believe also that many patients would have done better if two or more injections of even 5 mg. per kilogram had been administered, but on the other hand a few remarkable results have been obtained by multiple small doses.

Reactions.—In some cases even large doses, 5 mg. per kilogram or over, have been followed by little or no reaction. In most cases there is a definite and often very pronounced reaction, consisting of an immediate slight depression, a feeling of discomfort in the upper part of the abdomen and perhaps a slight headache, followed shortly afterward by nausea, slight or pronounced, and a little later by bowel movements; the latter, however, are often absent. In febrile cases and in most others, there is a rise in temperature varying from 1 to 5 degrees, which usually comes on within from three to four hours after the injection. In some cases this is accompanied by a chill, which is rarely very severe. In one case a temperature rise to 107.5 was recorded, and the patient recovered. The initial rise in temperature is almost always followed by an early and very profound drop, not infrequently to normal or nearly so. In rare instances there is a fairly profound shock following the injection. Cases are recorded in which the pulse has become very bad, the patient cold and clammy, and the shock so severe that restoratives were immediately required. We have been able to find only two deaths that can possibly be attributed to the drug. These are so important that we have given them in detail.

As noted above, it is impossible to say whether these patients died as a result of the injection of mercurochrome. It seems almost certain that both of them would have died without the injection, and the case of the boy, which looks to us like one of embolism, might have ended as it did at any time. In the second case, presumably incurable pemphigus, the reaction was evidently so severe as to hurry the death of the patient. The following paragraphs show the effect of the reaction in detail:

Therapeutic Effect of Injections.—In the cases that have been cited in great detail, and in the tables and analyses that have accompanied them, we have already stated at length the results that may be obtained in certain cases with mercurochrome-220 soluble given intravenously. The records cited, while often brief, are definite in showing that, in such diseases of the skin as erysipelas, furunculosis, cellulitis and infections of the soft parts, including abscesses, very rapid clearing up of the infectious process often follows intravenous injections of mercurochrome-220. In arthritis, the disappearance of pain, swelling and limitation of motion has also in some cases been extremely striking. Under the septicemia group, we have recorded fourteen really amazing recoveries, and in pneumonia, particularly in children, a limited number of really striking results have been cited.

Freeman and Hoppe seem justified in the claim of having reduced the mortality in pneumonia in children from 39 to 8 per cent., in a series of forty-six cases. If the results here recorded are borne out in the future, a very considerable lowering of the mortality rate in certain types of pneumonia may occur. Pneumonias due to *Streptococcus hemolyticus* seem to be more amenable to the treatment, but we have records also of pneumococcus cases.

In the treatment of gonorrhea and its complications, the recorded experiences are still too meager to warrant sweeping deductions. There have been many failures, generally due, we believe, to insufficient treatment or to the early development of reactions that prevented continuation of treatment. When the patient has been able to take a full series of fairly large doses, very definite sterilization of the local lesion and pronounced effect on the complications has sometimes occurred. Too much cannot be expected in chronic gonorrhea associated with lesions of long standing, strictures, ulcerations, prostatitis, etc. Even though intravenous therapy is employed, one is not justified in not using in addition well tried, old methods; and some of our experiences would seem to indicate that gonococci and other bacteria may remain in the urethra or other urinary passages after having been eliminated from the tissues, so that local treatment may be absolutely necessary to produce sterile cultures.

In chronic urinary infections there have been some successes and many failures.

As to the use of mercurochrome-220 in some of the infectious and contagious diseases that have been cited above, the recorded cases are still too limited to warrant any conclusions, except that the use of the drug has not apparently been associated with any untoward effect, and the results obtained have been sufficiently encouraging to warrant further trial. Its use in typhoid carriers seems warranted by the very favorable results of the experiments cited. In cases with prolonged septic temperatures, a few striking results have been obtained.

A study of the charts and case histories shows a quite typical temperature reaction—an initial rise followed by a rapid fall to normal or below, often with no further pyrexia or much less than before the injection. This is the most striking feature of what we might call the intravenous germicide reaction. Much study will be required to reach more than hypotheses in regard to this basic problem of chemotherapy. It is probable that the direct action of the drug on the bacteria in the blood stream or in local lesions is only one of the many factors involved. But the reaction is so definite and so immediate that no one can gainsay its important relationship to the remarkable changes in the clinical condition which usually follow an intravenous injection of mercurochrome-220 soluble.

We realize that, in thus presenting a new form of therapeutics in such a varied series of cases, we will encounter much criticism and perhaps be accused of presenting a panacea for every infectious disease. We are quite willing to meet this criticism with the series of cases here recorded, which we believe justifies the final assertion that in mercurochrome-220 soluble, intravenously administered, a really remarkable addition to therapeutics may be claimed. It is a drug the usage of which in a great variety of septic conditions seems justified. Further progress toward a "therapia sterilisans magna" has been made.

THE EFFECT OF THE UNIT RECORD SYSTEM AND IMPROVED ORGANIZATION ON HOSPITAL ECONOMY AND EFFICIENCY*

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One of the improvements in hospital service which have been especially urged on boards of managers within recent years is the keeping of good records, and in particular the establishment of a record system that will enable the institution to keep together all the information regarding each patient, whether the patient has been treated in the outpatient department, in the ward, or in different branches of medical or surgical services. Close relation between members of the staff organization, and particularly between the inpatient and the outpatient services, such as exists between the different branches of the hospital, has also been urged as a means of promoting a uniform and continuous policy in regard to the treatment of the patient.

The Presbyterian Hospital, with a few other institutions in this country, has taken the lead in establishing unit record systems and in taking steps toward unified staff organization. It was desirable to ascertain how far these changes, introduced during recent years at the Presbyterian Hospital, can be demonstrated to have improved the service to the patient; and how far these changes have affected, if at all, the economy of hospital management.

The Committee on Dispensary Development of the United Hospital Fund, being interested in these subjects from the standpoint of the outpatient department, as well as because of their general bearing on hospital improvement, agreed to finance a statistical study to be made at the Presbyterian Hospital. With the approval of the hospital authorities, under the oversight of Doctor Allen O. Whipple, Director of Surgery, and of Mr. Michael M. Davis, Jr., Executive Secretary of the Committee, I was engaged by the Committee to make a study of a series of records, in the endeavor to shed light on these questions.

METHOD OF STUDY

From the diagnostic index of the hospital, three series of cases were selected, i. e., hernia, ulcer (gastric or duodenal) and chronic appendicitis; only the records of ward patients were included. Equal numbers of records in each series were selected from three periods of time during

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*Report of a study made at the Presbyterian Hospital, New York City, under the auspices of the Committee on Dispensary Development of the United Hospital Fund.

recent hospital history: (a) the period before 1915, when the unit system of records had not been established, and when no follow-up clinic existed; (b) the period from 1916 to 1921, when the unit record system had been established and a follow-up clinic was in operation, through which the results of surgical treatment would be ascertained; and (c) the period from 1921 to 1922, when a close relationship had been established between the inpatient and the outpatient departments by a diagnostic clinic in the outpatient, through which admissions to the surgical ward of the hospital took place, and in which members of the senior staff of the hospital, as well as their assistants, gave regular service.

Three hundred cases of indirect, inguinal, reducible hernia were selected, one hundred from each period; sixty cases of gastric or duodenal ulcer, twenty from each period, and sixty of chronic appendicitis, similarly divided. It was necessary to examine over two thousand records for the purpose of making this selection, in order to eliminate cases with complications. Thus, of the hernia series, no cases are included which presented such complications as temperature or other evidences of infection, or in which other diseases were present.

When the selection had been made, each series of records was carefully studied, certain tabulations were made, and comparisons were then instituted between the three periods. The results of these studies are summarized in this article, together with a general statement of the findings and conclusions.

CASES OF HERNIA

Comparison of Records in the Three Periods.—First Period: As far as histories are concerned, some of the first period records are occasionally more intelligent, as far as the method of the bringing together and the correlation of facts is concerned, and are more complete than some very recent ones, in which quantity is sometimes a feature, but in which the quality is not of a kind to be approved. What strikes one in the records of the first period is the lack of laboratory findings. In some cases, laboratory work was apparently done without any system; urinalysis, particularly, appears to have been conducted without any apparent system. The number of blood examinations made during the first period is small. In 100 cases, only four blood examinations were made. Urine examination sheets do not always give exactly the data expected; microscopic findings are frequently disregarded, and often the specific gravity column does not serve its purpose. Records of anesthesia cannot be found in the majority of cases. Patients appeared in the ward without any note of admission, except in a very few cases from a private physician who merely diagnosed the case and requested surgical intervention. If the patient was readmitted and the

surgeon desired to find out what the results of the examination were at the time of the first admission, he was forced to rely chiefly on the patient's narrative or to search through huge volumes of records in order to find the previous notes. Even this undertaking was not often crowned with success. The temperature chart was very badly printed and rather annoying to the reader. That is about all that is worth while mentioning in regard to the records of the first period.

As to the patient who was supposed to derive benefit from the institution, it may be said that certain results were achieved, operations were performed, observations of postoperative periods recorded, and, at the end of a certain number of days, the label "cured" was attached. This gave the patient the right to leave the hospital, thus closing the case as far as the institution was concerned, but not very often closing the subject of treatment. The average number of hospital days is quite high compared with those included in the period which followed. In some cases, the hospital stay was prolonged for no reason at all. The

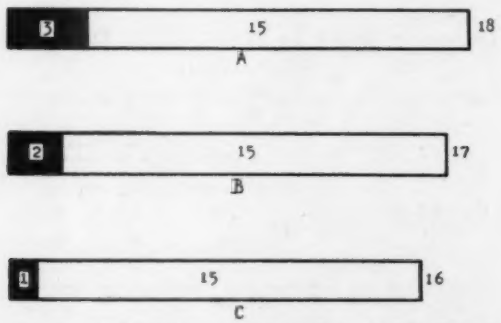

Fig. 1.—Diagram to illustrate the decrease in the average number of days' stay in the hospital for patients with hernia: *A*, first period; *B*, second period; *C*, third period. Black spaces represent preoperative stay; white spaces, postoperative.

preoperative stay was unnecessarily long, and it was not long because of the laboratory work performed; neither was it justifiable, in the case of simple hernia, by the necessity of careful observation for the purpose of diagnosis. The only explanation to be offered is that the stay was prolonged because of the schedule of the operating room or the convenience of the operating program of the attending surgeon.

Second Period: With the introduction of the follow-up clinic and unit history system, great improvement may be observed, the patient and the institution both being benefited by it. A separately bound volume for each patient admitted to the hospital is a reference book in which may be found without delay at any time the desirable notes and findings, even if the patient was readmitted several times. This step meant considerable time saving for the surgeon who attempted to study the history

of the patient before he was admitted. This method also saved the time of the surgeon in the outpatient department, who, when learning from the patient of a previous admission to the hospital, requests the history from the record room and has before him a complete record of the case. This was impossible in the first period. When, for instance, I made an effort to find some records of a patient before his admission to the hospital during the first period, only a few short notes could be obtained with merely the patient's name, address, age, and diagnosis of the case so hastily recorded that they were of no practical value. The histories of the second period were themselves far more complete. The first page, providing for the recording of general information in regard to the patient, is typewritten, although clerical carelessness in the filling out of this information was observed. The second page is devoted to the record of the procedure in the outpatient department, but the record of laboratory work is omitted. The third page contains the record of the operation and includes a history of

TABLE 1.—*Laboratory Work on Hernia Cases During Each of the Three Periods*

	Number of Cases	Laboratory Work			Average Number of Outpatient Department Visits
		Wassermann	Dental Clinic	Pathology	
First period, before the unit system	100	2	0	0	0
Second period, during the unit system and follow-up clinic	100	42	8	68	4
Third period, diagnostic clinic	100	98	100	97	3

anesthesia and surgical procedure, together with a report of the laboratory work, which is more complete than that recorded during the first period.

Third Period: The records of the last period, in which the diagnostic clinic was established, show even more improvement, among which may be noted the substitution of the word "improved" for the word "cured," which was formerly used. Table 1, which summarizes the laboratory work done during the three periods, furnishes evidence of this improvement.

Number of Days' Stay in the Hospital.—Table 2 reveals the interesting fact that the average number of days which the patient spent in the hospital diminished in each period from eighteen in the first and seventeen in the second to sixteen in the third. Perhaps of more significance is the diminution of the maximum number of days, that is, the case of longest stay, which, it will be seen in the table, drops from twenty-four to eighteen. The minimum number of days remains constant throughout the three periods, at fourteen days.

TABLE 2.—*Number of Days' Stay in Indirect Inguinal Hernia Cases (Reducible) at the Presbyterian Hospital, 1911-1923*

	Number of Cases	Total Hospital Days			Preoperative Hospital Days			Postoperative Hospital Days		
		Maximum	Minimum	Average	Maximum	Minimum	Average	Maximum	Minimum	Average
First period, before the unit system....	100	24	14	18	6	1	3	18	13	15
Second period, during the unit system and follow-up clinic	100	20	14	17	4	1	2	16	13	15
Third period, diagnostic clinic	100	18	14	16	2	0	1	16	14	15

TABLE 3.—*Total Number of Days Spent in Hospital, Classified by Number of Preoperative Days, by Patients Operated on for Inguinal Indirect Reducible Hernia*

1911–1914

Total Days	Preoperative Days							Total
	0	1	2	3	4	5	6	
13	..	..	..	..	..	..	..	..
14	..	1	..	..	..	..	..	1
15	..	..	..	..	..	..	..	..
16	..	..	3	1	..	..	..	4
17	..	..	7	7	3	..	..	17
18	..	2	16	30	7	..	..	55*
19	..	..	5	10	4	1	..	20
20	..	..	1	..	..	..	1	2
21	..	..	1	..	..	..	..	1
22	..	..	..	..	..	..	..	..
24	..	..	..	..	..	..	1	1
Total	..	3	33	48*	14	1	2	101

1915–1920

Total Days	Preoperative Days							Total
	0	1	2	3	4	5	6	
13	..	..	..	..	..	..	..	..
14	..	3	..	..	..	..	..	3
15	..	13	5	..	..	..	..	18
16	..	9	7	1	..	..	..	17
17	..	13	11	4	..	..	..	28*
18	..	1	7	5	2	..	..	15
19	..	1	5	6	2	..	..	14
20	..	..	1	3	2	..	..	6
21	..	..	..	..	..	..	..	..
22	..	..	..	..	..	..	..	..
23	..	..	..	..	..	..	..	..
Total	..	40	36*	19	6	..	..	101

1921–1923

Total Days	Preoperative Days							Total
	0	1	2	3	4	5	6	
13	..	..	..	..	..	..	..	..
14	2	..	..	..	..	..	..	2
15	11	22	..	..	..	..	..	33
16	7	28	15	..	..	..	..	50*
17	..	8	6	..	..	..	..	14
18	..	..	1	..	..	..	..	1
19	..	..	..	..	..	..	..	..
20	..	..	..	..	..	..	..	..
21	..	..	..	..	..	..	..	..
22	..	..	..	..	..	..	..	..
23	..	..	..	..	..	..	..	..
Total	20	58*	22	..	..	..	..	100

* Middle cases.

More significant, however, than the total number of days' stay in the hospital is the division into preoperative and postoperative stay. It will be observed in the table that the average number of preoperative days drops from three to one, and the maximum from six to two. The average length of the postoperative stay remains constant.

The contrast between the three periods is more clearly shown in Table 3, which gives the details and does not depend merely on the average figures. A glance at this table shows that there is not only a steadily progressive reduction in the number of preoperative days, but that there is also a reduction in the total number of days spent in the hospital and in the scattering of the cases. In the third period, the work approaches a standardized procedure.

This classification by postoperative days is also shown in Table 4. The entire range in the third period is between fourteen and sixteen days, instead of between thirteen and nineteen days as in the first period and thirteen and eighteen days in the second.

TABLE 4.—*Postoperative Days for Cases Recorded in Table 3*

Days	1911-1914	1915-1920	1921-1923
13	5	9	..
14	19	26	39
15	41	27	45*
16	26	28	16
17	7	9	..
18	2	2	..
19	1	..	..
20	..	....	..
Total	101	101	101

* Middle cases.

CASES OF ULCER AND APPENDICITIS

Only sixty cases belonging to each group are included in this series, twenty from each period. The number, like the number of cases of chronic appendicitis, is too small to carry as much weight as does the longer series of hernias, but the figures will be suggestive and, as will be seen, are confirmatory.

First Period: The patient was admitted to the hospital, operated on, in a great majority of cases, within twenty-four hours, remained in the hospital for ten or eleven days in cases of appendicitis and from fourteen to seventeen days in cases of ulcer, and then having been labeled "cured," or, in very exceptional cases, "improved," left the institution, and the case was closed, as far as the hospital was concerned. Most of these patients, during the first period, were admitted through unknown channels; previous histories, either in connection with the outpatient department or elsewhere were not known, so that duplication in histories, laboratory work, etc., could not be studied. The completeness and subject matter of the records varied with the individual surgeon.

Second Period: The introduction of the unit system of records and the follow-up clinic seems to have improved the situation so markedly that this period represents a striking contrast with the first. The appearance of the patient in the ward was usually preceded, as the record shows, by an examination in the outpatient department, and a certain amount of laboratory work was done. In the record there appear new pages, e. g., printed questionnaires for cases of chronic appendicitis, the report of the dental clinic, the house surgeon's resumé, in addition to the recording of much more thorough laboratory work, including the reports, Wassermann reactions and roentgen-ray findings. There appears to be some duplication in the recording of histories, laboratory findings, etc., which may be due either to the failure to study the case thoroughly in the outpatient department, or, as in some instances seemed apparent, to the simple matter of tradition in ward routine.

TABLE 5.—*Laboratory and Other Work Done in Cases of Chronic Appendicitis, of Gastric Ulcer and of Ulcer of the Duodenum*, 1911-1923

	Chronic Appendicitis						Gastric Ulcer and Ulcer of Duodenum					
	Number of Cases	Follow-up	Outpatient Department Visits	Wassermann	Dental Clinic Prophylactic	Results Recorded	Number of Cases	Follow-up	Outpatient Department Visits	Wassermann	Dental Clinic Prophylactic	Results Recorded
First period, before unit system.....	20	0	4	1	0	0	20	0	0	4	0	0
Second period, during unit system and follow-up clinic.....	20	18	15	10	4	16	20	16	16*	19	10	18
Third period, diagnostic clinic.....	20	20	13†	14	20	12‡	20	18	18	20	20	10§

* Four patients were admitted from the emergency ward.
† Seven patients were admitted from the emergency ward.
‡ Still under observation.
§Another patient still under observation.

There are indications that the follow-up clinic was of great importance to the service. After discharge from the ward, the patient remained for some time under the observation of an attending surgeon, who had the opportunity to study the results of the treatment at first hand, in some cases for years. All his appears in the record.

In this period, the term "cured" was in the process of being discarded, and the word "improved" substituted.

Third Period: The records indicate that the establishment of the diagnostic clinic brought about further improvement. There is greater completeness of records; the routine use of Wassermann tests, oral prophylaxis, and a complete roentgen-ray diagnosis are noticed.

These changes are shown statistically in the following tables. Table 5 indicates the great increase in the amount of laboratory work as well as in certain other work done during the three periods.

Table 6 shows duplications that were estimated to have occurred during the three periods.

TABLE 6.—*Duplications of Histories and Tests in Cases of Chronic Appendicitis, of Gastric Ulcer and of Ulcer of the Duodenum*, 1911-1923

	Chronic Appendicitis				Gastric Ulcer and Ulcer of Duodenum			
	No. of Cases	Physical History	Laboratory	Roentgen Ray	No. of Cases	Physical History	Laboratory	Roentgen Ray
First period, before unit system	20	0	0	0	20	0	0	0
Second period, during unit system and follow-up clinic	20	11	11	1	20	13	13	5
Third period, diagnostic clinic	20	10	13	4	20	6	8	3

The effect on the number of days' stay in the hospital, according to Tables 7 and 8, appears to be negative. There is an actual increase in the second period in both appendix and ulcer cases, which may be interpreted as being the result of a more careful study of the case. In the ulcer cases, a slight diminution of the average number of hospital days appears in the third period, and there is a reduction in the maximum number of preoperative days in both groups.

TABLE 7.—*Chronic Appendicitis*

		Total Hospital Days			Preoperative Hospital Days		
	No. of Cases	Maximum	Minimum	Average	Maximum	Minimum	Average
First period, before unit system	20	26	10	13	5	Hrs.	2
Second period, during unit system and follow-up clinic	20	23	12	16	10	Hrs.	3
Third period, diagnostic clinic	20	24	12	16	6	Hrs.	4

TABLE 8.—*Gastric Ulcer and Ulcer of the Duodenum*

		Total Hospital Days			Preoperative Hospital Days		
	No. of Cases	Maximum	Minimum	Average	Maximum	Minimum	Average
First period, before unit system	20	40	14	20	7	1	3
Second period, during unit system and follow-up clinic	20	41	18	27	16	1	6
Third period, diagnostic clinic	20	36	20	26	15	2	6

The two final tables (9 and 10) show the number of visits made by patients to the outpatient department before their admission to the ward, the number of visits to the outpatient department after their discharge, for which the follow-up clinic was responsible, and the diagnostic errors observed (difference between preoperative and postoperative records). It will be seen that the total number of visits made before admission by the twenty patients with gastric or duodenal ulcer in the second

period (the first period being discarded on account of lack of data) is seventy-three. This means that the average number of visits to the outpatient department made by each patient before the final decision as to the mode of treatment was reached, was from three to four. Considering the insignificant number of cases analyzed, the economic gain is quite evident. The clinical staff is able to be of assistance to a larger number of patients during the same period of time; this is the result of improved clinical methods of diagnosis, which frequently leads to more efficient and radical treatment, whereby the patient does not have to be kept under observation for an extended period of time. The same interpretation may be put upon the reduced number of follow-up visits to the outpatient department during the third period.

A marked decrease in diagnostic errors in the third period is observed in both ulcer and appendix cases, indicating that there has

TABLE 9.—*Chronic Appendicitis*

	Number of Cases	Total Number of Outpatient Visits Before Admission	Total Number of Outpatient Visits After Discharge (Follow-up)	Diagnostic Errors
First period, before the unit system	20	..	..	3
Second period, during the unit system and follow-up clinic	20	48	72	1
Third period, diagnostic clinic	20	38	45	0

TABLE 10.—*Gastric Ulcer and Ulcer of the Duodenum*

	Number of Cases	Total Number of Outpatient Visits Before Admission	Total Number of Outpatient Visits After Discharge (Follow-up)	Diagnostic Errors
First period, before the unit system	20	..	..	4
Second period, during the unit system and follow-up clinic	20	73	94	2
Third period, diagnostic clinic	20	45	78	0

been improvement in the standard of clinical examination. The diminution is striking, particularly in the ulcer cases. The records of chronic appendicitis are not of as much clinical significance because of the fact that one is seldom able to diagnose such a condition correctly and it is left to the follow-up clinic to determine the correctness of preoperative and postoperative findings.

SUMMARY AND CONCLUSIONS

The limitations of such a study as the preceding should be borne in mind, for the number of cases in relation to the entire hospital intake is very small. The hernia cases present a surgically clearcut group, more so than the ulcer and appendicitis cases, and for that reason perhaps more weight can be attached to the hernia statistics. It is fair to add

that very great care was given to the selection of cases, and that effort was made to avoid a selection which would bias the result, or which would include the same group cases which were surgically not comparable with the others.

The situation at the Presbyterian Hospital is complicated by the presence of teaching, through the hospital's affiliation with the Columbia University College of Physicians and Surgeons. The presence of students and the use of cases for teaching purposes has some effect on the diagnostic procedure and on the elaborateness of the records, as compared with that of non-teaching institutions. On the other hand, the comparison of the three periods at the Presbyterian Hospital is probably little influenced by this factor, since teaching has been conducted throughout these periods.

On the whole, even with the foregoing limitations in mind, one cannot avoid coming to the conclusion that a very great improvement in service to the patient is apparent during these years, that this improvement has been accompanied by a shortening of the patient's stay in the hospital, and consequent economy in hospital service and expense. There are occasions in which a brief stay in bed for diagnostic purposes is a medical and financial economy both to patient and hospital, enabling a diagnosis to be promptly and accurately established without a prolonged and sometimes dubious study of an obscure ambulatory case. In the case of hernia, such instances are very rare.

To a certain extent, the decrease in the number of days during which the patient has to be cared for in bed has been made up for by additional attention to the patient in the outpatient department. The cost of an outpatient visit, however, averages about one-fifth that of a day's care in bed. To the hospital, therefore, the transfer of a certain amount of work to the outpatient department is financially advantageous, while to the patient the transfer means that, in many instances, work or the usual household activities can be resumed without the additional loss and interruption to family life occasioned by the days spent in a hospital bed.

How far these gains in efficiency and economy can be attributed directly and solely to the establishment of the unit record system, to the follow-up clinic, diagnostic clinic, etc., should be considered. General advances in surgery and in hospital administration must not be forgotten. Nevertheless, the three changes mentioned have been outstanding alterations in the Presbyterian service, and it is fair to attribute at least the major influence to them. Furthermore, the detailed study of the records bears out this point.

EXHAUSTION

VIII. ANAPHYLAXIS; PREGNANCY

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The close accordance of the symptoms of anaphylaxis with those of autointoxication, especially with those of protein intoxications, led to the belief that whatever the intermediate or concurrent effects of the anaphylactic reaction on the system as a whole, the primary cause of the end-results would be found to be identical with that to which we have attributed the end-results of the injection of peptone or other toxic agents, and with other causes of general exhaustion; that is, the belief was that, in their fundamental characteristics, anaphylactic shock and traumatic shock would be found to be identical.

The complex chemical pathologic changes which accompany pregnancy with the associated metabolic disturbances make it seem appropriate to include in this section certain studies of pregnant animals.

A. HISTOLOGIC STUDIES

Injection of Ox Serum.—In two experiments, after the intravenous injection of 2 c.c. of ox serum, all the brain cells were found to be fatigued. Unfortunately, the record of these experiments, the primary purpose of which was to test the suprarenal output, does not state the length of time between the injection and the death of either animal.

Injection of Sheep Serum in a Previously Sensitized Animal.—An hour and a half after the intravenous injection of 20 c.c. of sheep serum in a dog sensitized one month previously by the subcutaneous injection of 5 c.c. of serum, all the brain cells were found to be fatigued.

To each of two other dogs which had received a preliminary sensitizing dose of serum thirty-three days previously were given, respectively, 4 and 5 grains of morphin an hour before the intravenous injection of 20 c.c. of sheep serum. In marked contrast to the results of the previous experiments, most of the brain cells of these animals were markedly hyperchromatic.

Pregnancy.—The histologic effects of pregnancy both before and after delivery are given in Table 1 (Fig. 1). An extract was made from the placenta of Cat 1, 10 c.c. of which was injected into another cat. The histologic findings in this animal are also included in Table 1. Examination of other organs and tissues besides the brain showed no significant change.

TABLE 1.—*Histologic Effects of Pregnancy and of the Injection of Placental Extract* *

Experiment	Protocols	Cerebrum	Cerebellum	Liver	Suprarenals
1	Cat: period of pregnancy approximately three weeks	Some active cells; nearly all fatigued	Some active cells; nearly all fatigued	Normal, no loss of cytoplasm	No apparent loss of cytoplasm from either cortex or medulla
2	Cat: Period of pregnancy approximately four weeks	Cells hyperchromatic and active	Cells hyperchromatic and active	.....	Uniform loss of cytoplasm in most of cortex; some cells vacuolated
3	Rabbit: full term	.....	All cells fatigued	Normal, no loss of cytoplasm	
4	Rabbit: killed eighteen minutes after delivery	All cells fatigued	All cells fatigued; some exhausted	.....	Normal
5	Cat: ether; four intravenous injections of placental extract, 10 c.c., at the following intervals: 30 min.; 20 min.; 15 min.; killed 3 hrs. after last injection	Nearly all cells fatigued	Some hyperchromatic and active cells; nearly all fatigued	Uniform loss of cytoplasm without vacuolation around periphery of lobule	

* Experiments by Dr. F. W. Hitchings; histologic examinations by Dr. J. B. Austin.

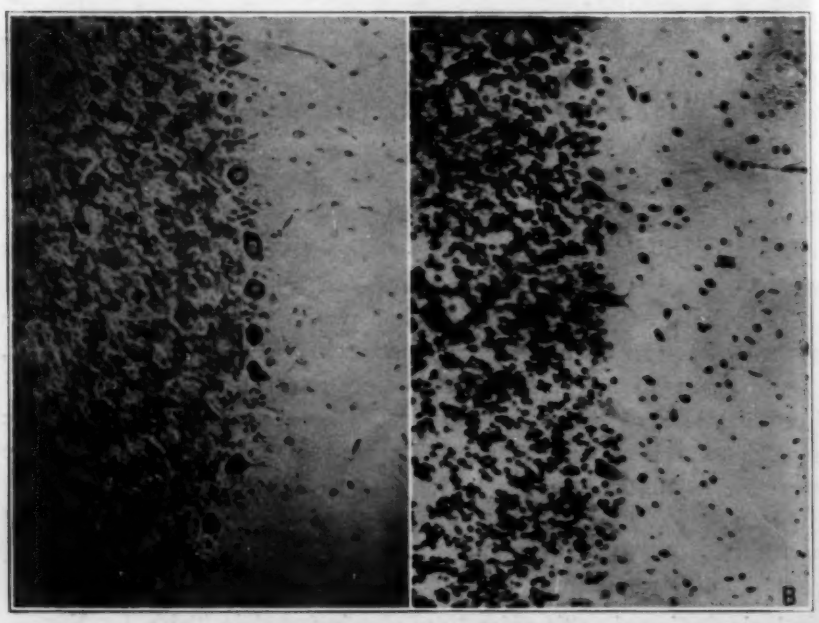

Fig. 1.—The effect of pregnancy on the cells of a cat; *A*, section of the cerebellum of a normal cat; *B*, section of the cerebellum of a cat immediately after delivery (reduced from photomicrographs × 310).

B. FUNCTIONAL AND BIOPHYSICAL STUDIES

Measurements of the Suprarenal Output.—Among four tests by Cannon's method of the suprarenal output after the injection of a foreign

TABLE 2.—*Effect of Anaphylaxis on the Suprarenal Output (Cannon's Test)* *

Experiment	Protocols	Epinephrin Test 1 (Control) Before Injection	Injection	Epinephrin Test 2	Epinephrin Test 3
	A. Foreign Serum in Normal Animal				
1	Cat: Ether.....	Negative	2 c.c. kitten serum	15 min. after injection, positive	Same sample 10 min. later, negative
2	Dog: Ether.....	Negative	15 c.c. ox serum	5 min. after injection, negative	(Few drops of epinephrin chlorid added to sample, positive)
3	Cat: Ether.....	Negative	2 c.c. ox serum	5 min. after injection, positive	Same sample 20 min. later, negative
4	Rabbit: Urethane.....	Negative	2 c.c. ox serum	5 min. after injection, positive	Same sample 25 min. later, negative
	B. Foreign Serum in Sensitized Animal				
1	Dog: Ether; sensitized 30 days before with 5 c.c. sheep serum	Negative	20 c.c. sheep serum	Sample 1, 20 min. after injection, positive Sample 2, 30 min. after injection, positive Sample 3, 1 hr. 5 min. after injection, positive	Sample 1, 50 min. later, negative Sample 2, 55 min. later, negative Sample 3, 30 min. later, negative
	C. Foreign Serum in Sensitized Animal after Morphin				
1	Dog: Ether; sensitized 33 days before with 1 c.c. sheep serum; morphin, 5 grains 1 hr. before experiment	Negative	20 c.c. sheep serum	10 min. after injection, negative	
2	Dog: Ether; sensitized 33 days before with 1 c.c. sheep serum; morphin, 6 grains 1 hr. before experiment	Negative	20 c.c. sheep serum	10 min. after injection, negative	
3	Dog: Ether; sensitized 33 days before with 5 c.c. sheep serum; morphin, 4 grains 1 hr. before injection	Negative	20 c.c. sheep serum	20 min. after injection, negative	
	D. Placental Extract				
1	Rabbit: Urethane.....	Negative	2 c.c. placental extract	5 min. after injection, positive	Same sample 25 min. later, negative

* Experiments by Dr. F. W. Hitchings.

serum, three were positive (Table 2, *A*); the injection of a foreign serum in a previously sensitized dog produced an increased output of

epinephrin (Table 2, *B*) (Fig. 2); but the output of epinephrin was not increased after the injection of a foreign serum in three sensitized animals which had received a preliminary dose of morphin (Table 2, *C*) (Fig. 3). One test of the output of epinephrin was made after the injection of placental extract, with a positive result (Table 2, *D*) (Fig. 4).

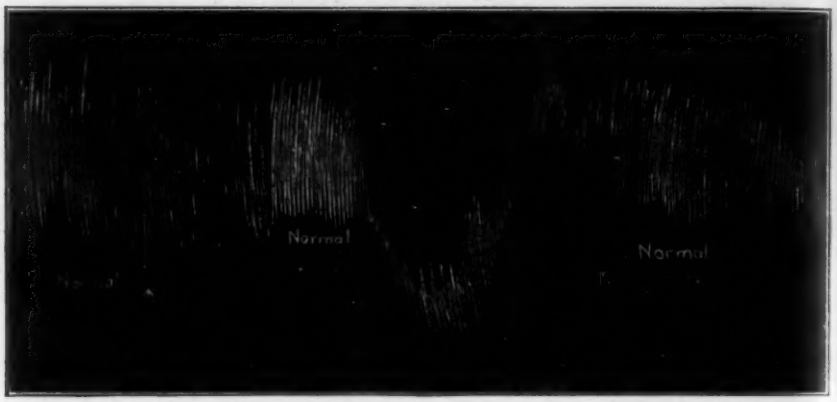

Fig. 2.—The effect of anaphylaxis on the suprarenal output; Cannon's test positive. Arrows indicate: (left), the addition of 5 c.c. blood from dog before anaphylactic dose was given; (center), blood from a dog in anaphylactic shock, 5 c.c.; (right), the addition of 5 c.c. blood from anaphylactic dog, after standing twenty-five minutes.

Fig. 3.—The effect on the suprarenal output of the injection of serum in a morphinized animal; Cannon's test, negative. The animal used in this experiment had been given 5 grains (0.4 gm.) morphin one hour before the peptone was injected. The arrows indicate: (left), the addition of 5 c.c. control blood from dog; (center), the addition of 5 c.c. blood from dog five minutes after intravenous injection of 15 c.c. beef serum; (right), the addition of a few drops pure epinephrin.

Electric Conductivity Measurements.—Electric conductivity measurements of the brain and the liver of each of three pregnant animals were made, the findings of which are given in Table 3 (Fig. 5). These findings are in accord with the histologic picture.

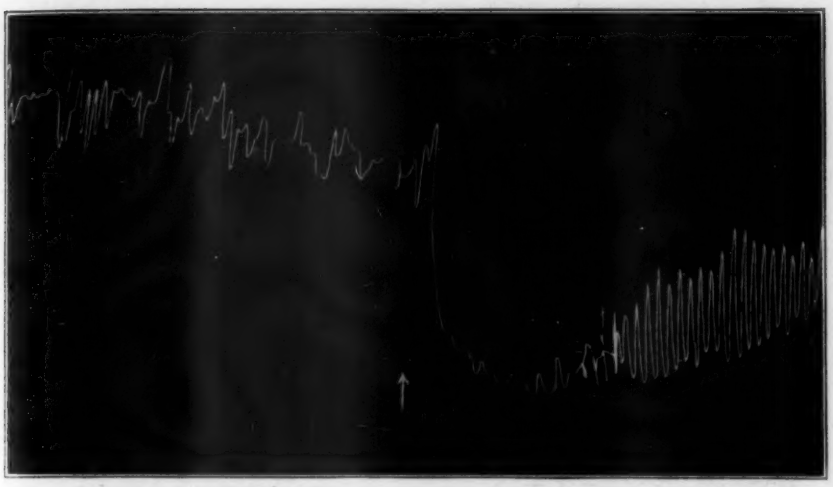

Fig. 4.—The effect of pregnancy on the suprarenal output; Cannon's test, positive; arrow represents the injection of 5 c.c. blood from a pregnant cat.

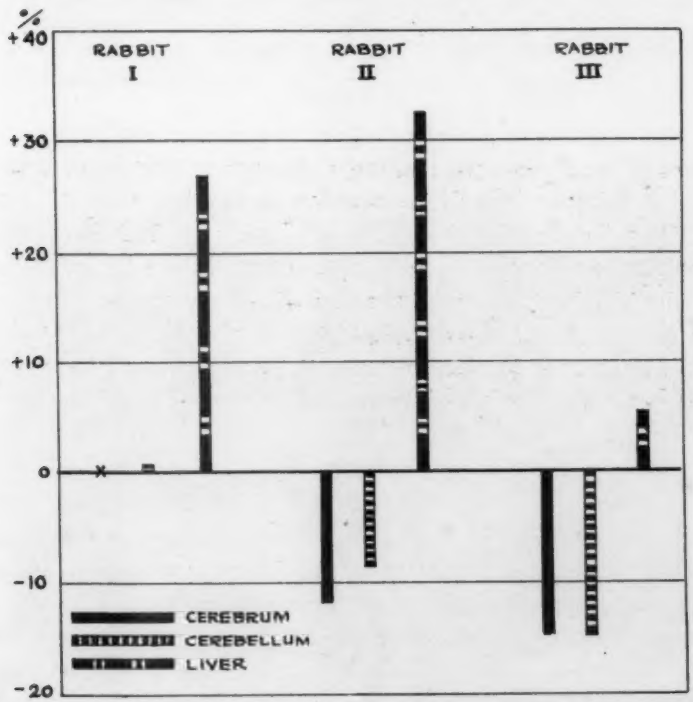

Fig. 5.—The effect of pregnancy on the electric conductivity of the brain and the liver: Rabbit 1, about twenty-one days pregnant; Rabbit 2, nearly full term; Rabbit 3, at term.

C. CLINICAL NOTES

Only one clinical note of value appears on the record of this group of experiments, but that one is significant. A marked and persistent typical anaphylactic fall in blood pressure followed the injection of sheep serum in a sensitized dog (Fig. 6, *A*). In the three animals morphinized before the injection, the blood pressure curve was altered as follows: In one, the fall was delayed for several hours following the injection; in another, there was a slight fall with a gradual return to the normal level; in the third, the characteristic fall was delayed about ten minutes (Figs. 6, *B* and 7).

TABLE 3.—*The Effect of Pregnancy on the Electric Conductivity of the Brain and the Liver* *

Date of Measurement	Cerebrum	Percental Deviation from Normal	Cerebellum	Percental Deviation from Normal	Liver	Percental Deviation from Normal
Normal group, 5/12-5/27/19....	00185	.....	00137	.....	00071	.....
Pregnant rabbits, 5/28/19						
1. About 21 days.....	00185	0.0	00138	+0.7	00090	+26.8
2. Nearly full term.....	00163	−11.9	00125	−8.8	00094	+32.4
Normal group, 10/17-10/27/19..	00168	.....	00134	.....	00094	.....
Pregnant rabbit, 10/19/19						
3. At term.....	00143	−14.9	00114	−14.9	00099	+5.3

* Experiments by Helen R. Hosmer and Amy F. Rowland.

SUMMARY

1. The injection of a foreign serum in a normal and in a previously sensitized animal produces histologic changes in the brain which are identical with those found in exhaustion from other causes.

2. The injection of a foreign serum in a morphinized animal does not produce any destructive histologic change in the brain.

3. The histologic changes characteristic of exhaustion are found in the brains of pregnant animals. Apparently, the extent of those histologic changes is in direct relation to the duration of the pregnancy and the general condition of the animal.

4. The suprarenal output is increased by the injection of a foreign serum, except in morphinized animals.

5. The electric conductivity of the brain and of the liver are altered by pregnancy, the conductivity of the brain being decreased and that of the liver being increased. The degree of change is apparently in direct relation to the duration of the pregnancy.

7. The anaphylactic reaction is marked by a characteristic fall in the blood pressure, except in morphinized animals when the alteration in the blood pressure is delayed or is atypical.

8. The findings in these studies indicate that the organs primarily concerned in the production of the phenomena forming the clinical

Fig. 6.—The effect of anaphylaxis on the blood pressure. Note the fall in the pressure at *A*, after an injection of serum immediately following an injection of morphin; compare with the lack of alteration in the pressure at *B*, three hours later. Arrows indicate: (left), intravenous injection of 10 c.c. sheep serum in dogs sensitized to same one month previously after the injection of 4 grains (0.26 gm.) morphin the same morning; (right) 10 c.c. again injected here (no fall three hours later).

Fig. 7.—Effect of anaphylaxis on the blood pressure of a morphinized animal. Note the lack of alteration in the pressure after the injection of the serum. Arrow indicates the intravenous injection of 12 c.c. of sheep serum into sensitized dog after the injection of 6 grains (0.4 gm.) morphin.

picture called "anaphylactic shock," as well as those characterizing the progress of pregnancy, are due to the same primary factor as that which causes the fundamental phenomena of traumatic or emotional "shock," i. e., exhaustion of the brain.

HYPERNEPHROMA AND CARCINOMA OF THE KIDNEY: A COMPARATIVE STUDY*

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ST. LOUIS

On account of the conflicting arguments placing a renal neoplasm under the classification of hypernephroma, considered here as arising from a suprarenal rest or a carcinoma, which we will consider as arising from kidney tubercular epithelium, I have attempted to find in the structure of the growth, gross and microscopic, sufficient similarity to its parent organ to suggest its origin. Sometime ago, I studied all the kidney tumors in the surgical pathology museum prior to 1921, some twenty-three in number, and placed four which had been diagnosed carcinoma with the hypernephromas. Of these twenty-three cases, I have been able to follow only twelve in all particulars. In the study of these twelve specimens, I have classified five as hypernephroma and seven as carcinoma. This classification was based wholly on their structure. To my great interest, it was later found that the patients whose disease was diagnosed as hypernephroma were still alive, except one who lived six years after his first symptom, while those classified as carcinoma are all dead (accompanying table).

Robin, in 1855, and Waldeyer, in 1867, first showed carcinoma of the kidney to be a proliferation of the tubular epithelium. In 1875, Sturm recognized the transformation of types of adenomas into carcinomas. Up to 1883, all renal carcinomas were believed to originate from tubular epithelium, although, in a very indefinite way, a yellow fatty tumor was recognized. In this year (1883), Grawitz showed that these tumors had a structure quite similar to that of the suprarenal cortex; later, proofs of the suprarenal rests were given. In 1892, Birch Hirchfeld gave to this group of tumors the term hypernephroma.

In recent years, although invoking the aid of chemistry, pathology and embryology, it has been impossible definitely to classify these tumors. Grawit's classification embraced a larger group than we accept, and he presented, as basic in favor of his group, their high cellular fat content with no degeneration, a fibrous core in the smaller tumors, a glandular cortex, their definite encapsulation and their subcortical location, where a majority of the suprarenal rests are found. Of late years, it sometimes seems that the term "hypernephroma" has been popularized to embrace almost all kidney neoplasms.

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*From the Department of Surgery, Washington University School of Medicine.

Some of the contentions against hypernephroma are: That at least many suprarenal rests are fatty renal epithelium; that papillary formation seen in hypernephromas is seldom seen in suprarenal tumors; that there may be more fat or glycogen (in gross) in carcinoma than in hypernephroma and vice versa, and, whether the lumina seen are true or false, in the latter case they are due to degeneration. It is probably true that fat is more uniformly distributed in the suprarenal rest tumors, but the chief point of differentiation is in their architecture, and it is suggested here that these neoplasms show constant similarities sufficient in all cases, both gross and microscopic, to point to their suprarenal rest origin.

GROSS EXAMINATION

The chief characteristic of hypernephroma is the friable, granular appearance, soft and cheesy in consistency, which is due, not to degeneration, but to the comparative absence of connective tissue. The capsule and septums are relatively thin. The lobulations and intrapelvic growth show this thin capsule, as there is less resistance offered at these points. On the other hand, given an outside resistant wall, the tumor is perfectly encapsulated. In its pelvic invasion it tries hard to retain its thin covering. Its characteristic color is a fatty yellow with occasional areas, lighter in color because of degeneration. There is also present a red and brown mottling due to hemorrhage, the depth of the color depending on whether the hemorrhage is recent or old. In contrast, see Figure 13 (Case 7) and Figure 11 (Case 6), cases of typical carcinomas, firm, smooth and not lobulated, showing a balance of growth of tumor cells, and contraction and resistance of the abundance of fibrous tissue; there is little hemorrhage, few or no cysts, and they are poorly circumscribed.

HISTOLOGIC EXAMINATION

Hypernephroma shows the cause of its friability in the small amount of fibrous tissue; the tumor is built by the growth of cell on cell, as stones are piled, their pattern of growth being determined by the ingrowth of the sinusoidal plexus. The clear cell papillary carcinoma may be quite definitely simulated in general architecture by the ingrowing of a hardy and abundant long-meshed capillary plexus where the cells are drawn to the endothelium. In a similar manner, by round meshed sinusoidal growth, an adenoma may be suggested. Both types frequently exist in the same neoplasm, and practically always the pattern of either type is completely lost in other areas of the tumor, where only sheets of large, clear, or finely granular cells with scattered blood vessels between and very little reticular tissue are seen. A suggestive adenomatous formation is sometimes observed, but, in these instances,

there remains the absence of fibrous tissue, which in the carcinoma circumscribes to some degree the type of growth formed by the inherent predisposition of the cell. This inherent predisposition shows, in the hypernephroma the structure of which may be called pseudocolumnar, simply a piling of cells, the arrangement of which depends on the ingrowth of a sinusoidal plexus. If the plexus be round meshed, the arrangement of cells may suggest the zona glomerulosa or reticularis,

Results of Operative Treatment *

Case No.	Age, Years	Sex	First Symptom	Mass Appeared	First Hematuria	Operation Date	Condition at Operation	Condition Since Operation
			Hypernephroma					
1	55	M	4 mos. with fever	2 wks.	48 days	1917	Lost 22 lbs.	Excellent
2	58	M	3 yrs. with hematuria	4 mos.	3 yrs.	1916	Good	Excellent
3	67	F	1 yr. with hematuria and colic	?	1 yr.	1920	Hb. 65%, some loss in weight	Excellent
4	62	M	6 mos. with mass in side	6 mos.	None	1920	Good	Excellent
5	50	M	6 yrs. with hematuria	1 wk.	6 yrs.	1920	Poor	Died at operation
			Carcinoma					
6	49	M	Lost 20 lbs. in past 4-5 mos.	2 mos.	7 wks.	1918	Poor, general carcinomatosis	Dead 3 mos. after operation
7	66	M	3 mos. pain in R.U.Q.	Indefinite mass	None	1918	Poor, general carcinomatosis	Dead 3 mos. after operation
8	5	M	2 mos. pain in R.U.Q.	3 wks.	....	1919	Poor, only fragments of tumor removed	Dead 1 mo. after operation
9	46	M	3 yrs. with hematuria	....	3 yrs.	1919	Poor, liver involved	Dead 3 mos. after operation
10	44	M	6 mos. pain in abdomen	4 mos.	3 mos†	1918	Poor, liver involved	Dead 3 mos. after operation
11	..	M	5 weeks‡	....	5 wks.	1913	Fair	Returned to clinic once, a year later severe pain in right hip, probably metastasis
12	..	M	13 months bleeding	....	13 mos.	1920	Poor	Dead 1 mo. after operation

* The ratio here, 5 hypernephromas to 7 carcinomas, gives an erroneous suggestion as to the frequency of suprarenal tumors since the remaining specimens not traceable in all particulars distinctly originated from renal tissue. The complete ratio would therefore be 5 hypernephromas to 18 carcinomas

† A small tumor in the left kidney had been confused with spleen for three months previous to admission to hospital.

‡ Adenocarcinoma.

or if it be long meshed, the zona fasciculata. Nowhere is this suggested origin constant in the same tumor; it varies with the erratic flow of the small vessels. The sinusoidal plexus varies markedly in its abundance.

In the adult suprarenal cortex, we recall that the cells have no basement membrane; they lie close to the endothelium of the blood vessels, and are separated in places only by a very slight amount of reticular tissue.

CONCLUSIONS

Kidney tumors arising from suprarenal rests are much less malignant than those arising from tubular epithelium, and the two types can be best differentiated by their gross appearance and histological structure, rather than by their location in the kidney, their chemistry or the conflicting embryological arguments.

SUMMARY

1. In twelve pathological specimens, the most recent removed three years ago, we find the mortality resulting from hypernephroma conspicuously lower than that resulting from carcinoma.

2. The hypernephroma is circumscribed by a relatively thin capsule, is friable, of a soft granular consistency, at times mottled red and brown in a soft yellowish mass and contains gelatinous cysts. Its outer walls are lobulated, the capsule thinning over these lobules as it does over the areas of intrapelvic invasion.

3. Histologically, the piled up, clear or finely granular cells are given shape, so that sometimes they resemble either the zona glomerulosa, fasciculata or reticularis, by the ingrowth of a sinusoidal plexus, or, in its absence, they remain broad sheets of cells with very little reticular tissue, divided irregularly by larger blood vessels.

4. Hypernephromas are less frequent than carcinomas.

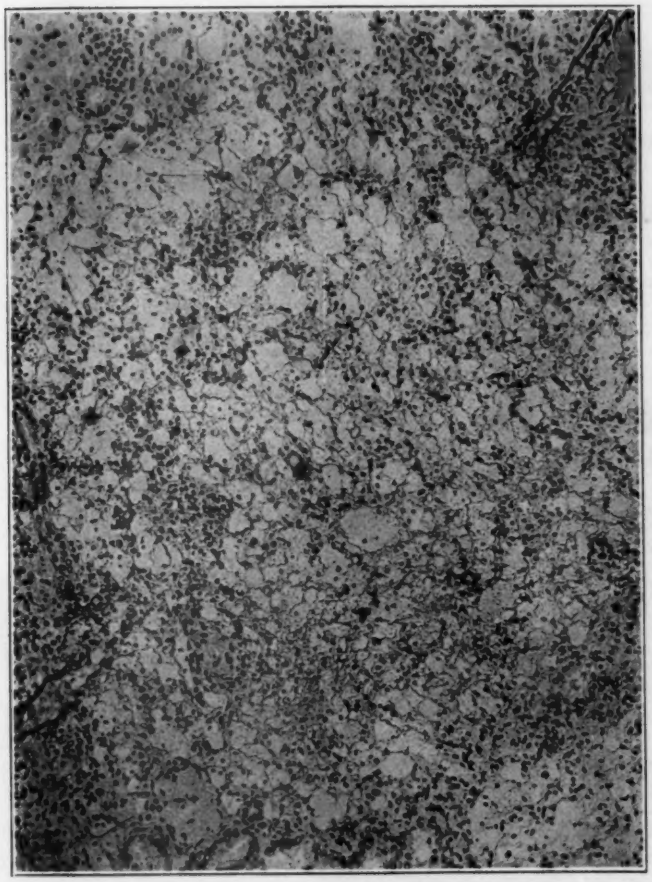

Fig. 1.—Suprarenal rest, with kidney tissue throughout; the cells are clear, lying in sheets with very little connective tissue, and that in scattered form.

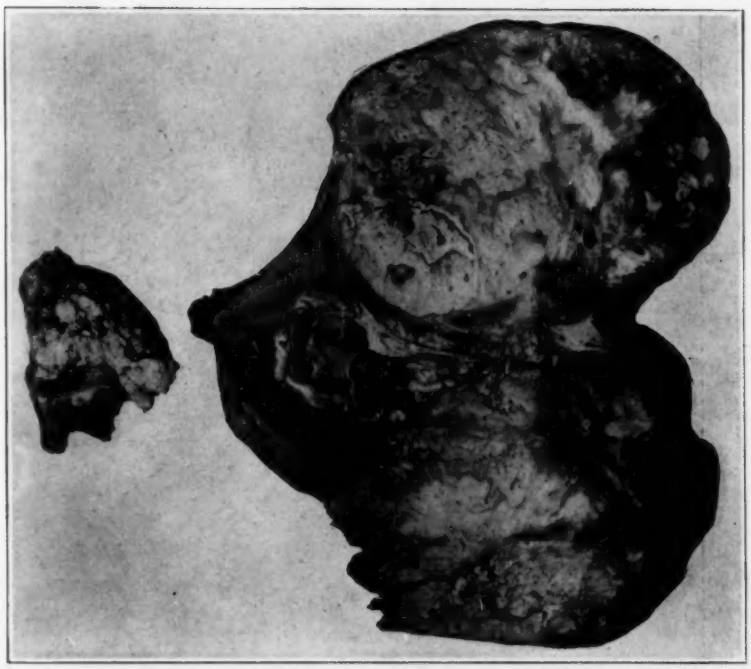

Fig. 2 (Case 1).—Friable, mottled, thin capsule, definitely circumscribed.

Fig. 3 (Case 1).—Large, clear cells in sheet formation; definite lack of fibrous tissue. It is such an area which, if invaded by a hardy capillary plexus, would form a tumor suggesting Figures 5 and 7.

Fig. 4 (Case 2).—Mottled thin capsule, with tumor invading pelvis and calices; a very typical hypernephroma.

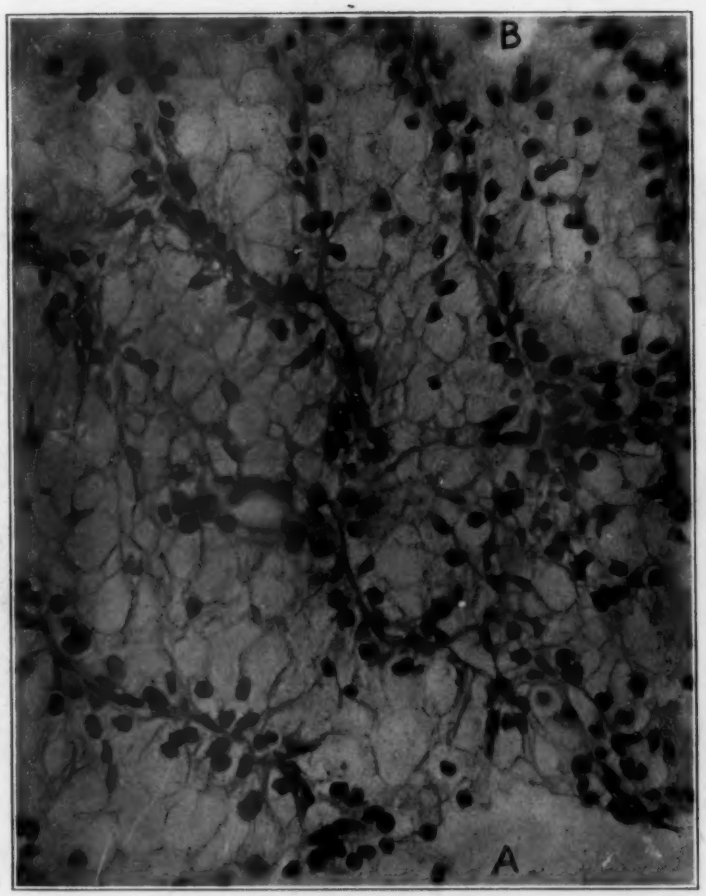

Fig. 5 (Case 2).—The cell outline shows a definite pull or elongation from A to B in the direction of the flow of vessels. This formation, suggesting a clear cell papillary carcinoma, is not constant throughout the tumor, but depends on the length and abundance of the capillary mesh; areas resembling those in Figures 3, 7 and 9 are easily found.

Fig. 6 (Case 3).—Soft, yellow, granular mass; no hemorrhage, very thin capsule and septums.

Fig. 7 (Case 3).—Columns of clear cells molded into definite alveolar formation by the ingrowth of round meshed capillary network, definitely suggesting an adenoma.

Fig. 8 (Case 4).—Notice the friability of the tumor, the mottling, the thin capsule and septums; location, upper pole.

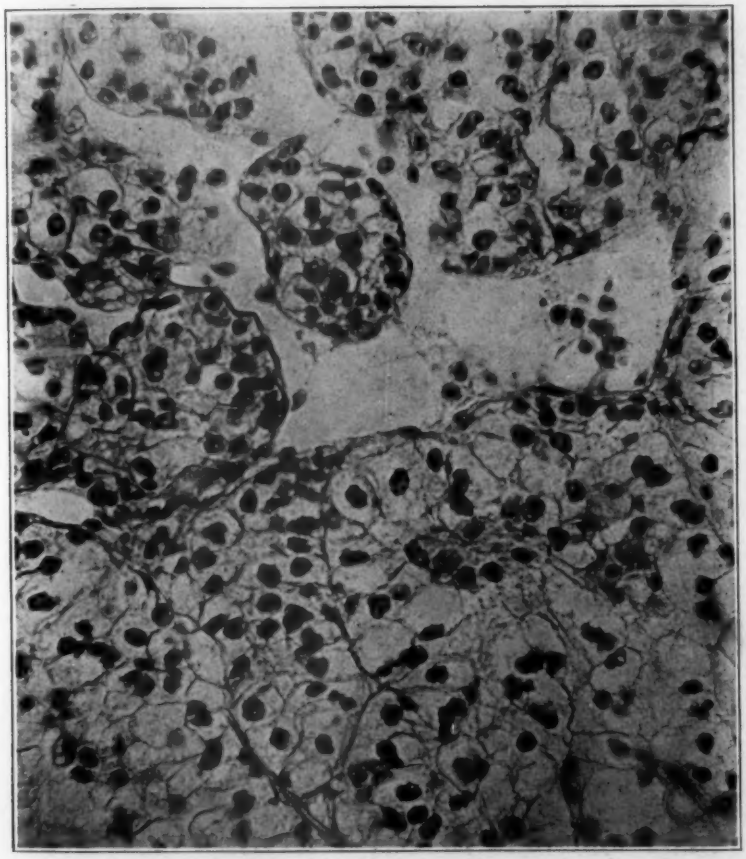

Fig. 9 (Case 4).—Large clear cells growing in sheets, with a definite paucity of reticular tissue; some 'adenoma' suggestion is produced in the upper portion of the picture by larger vascular spaces.

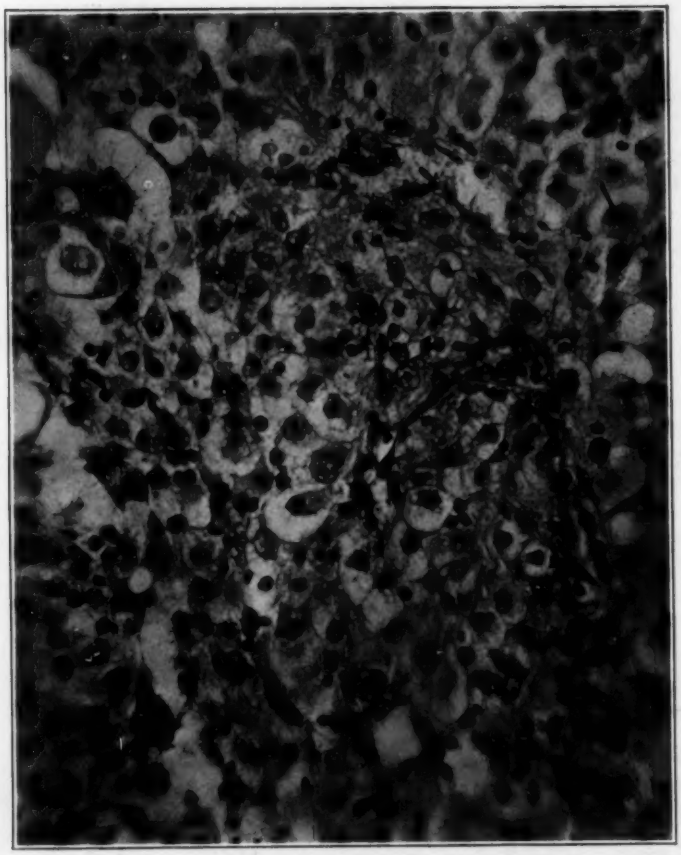

Fig. 10 (Case 5).—The cells are granular and clear, each cell lying free of reticulum and supporting its neighbor; the infection of long standing is shown by the small, round cell infiltration and fibroblastic formation and growth. Tumor not removed at operation.

Fig. 11 (Case 6).—Hard, white, smooth, infiltrating tumor.

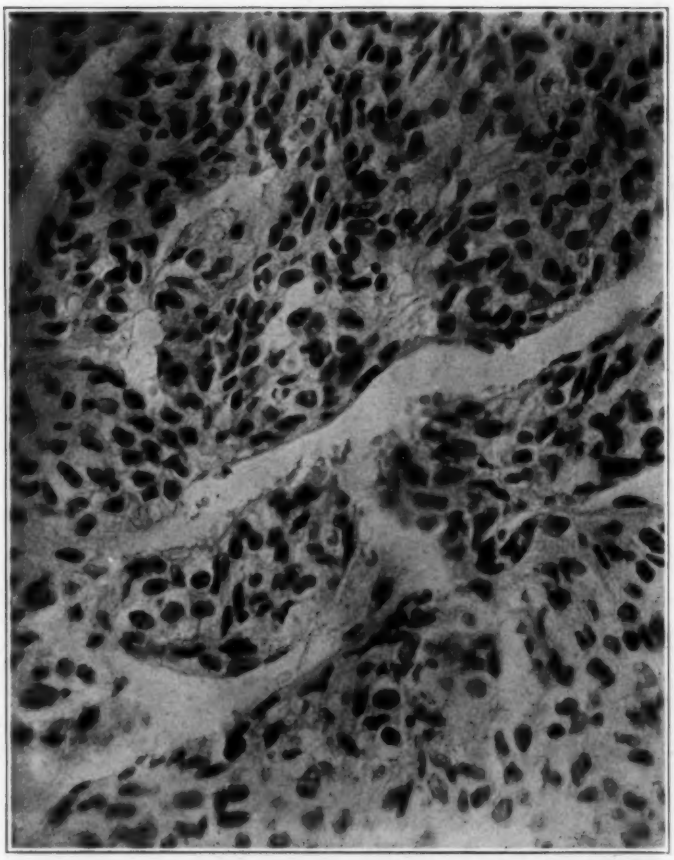

Fig. 12 (Case 6).—A very free fibrous tissue growth with comparatively little round cell infiltration.

Fig. 13 (Case 7).—Firm, glistening, white; pelvis compressed, no nodules, no hemorrhage. Definitely infiltrating.

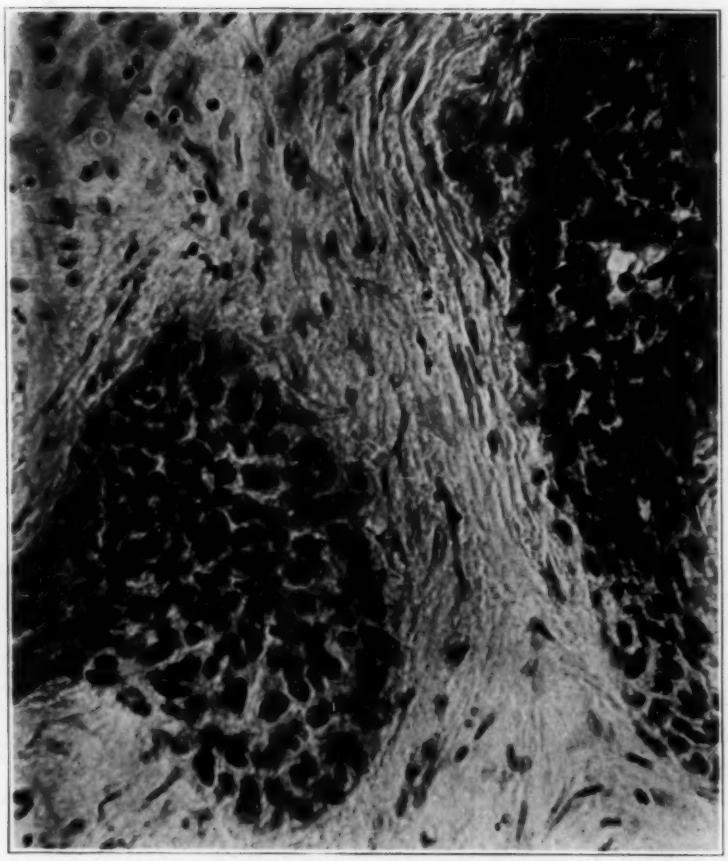

Fig. 14 (Case 7).—Typical infiltrating growth with dense connective tissue.

SEPARATION OF THE UPPER EPIPHYSIS OF THE RADIUS

ALBERT H. MONTGOMERY, M.D.

CHICAGO

Although injuries involving the elbow joint are very common, especially in children, separation of the epiphysis at the head of the radius is most infrequent. Because of the rarity of this lesion as well as its possible effect on the growth of the radius and the function of the elbow joint, the history of the following case may be of interest.

REPORT OF CASE

L. B., a white girl, aged 11 years, entered the Children's Memorial Hospital, Nov. 6, 1920. Five days before, she fell from a gymnasium ladder, a distance of 4 feet, and struck her left elbow on the floor. Pain and disability of the joint immediately followed the fall. The physical examination was negative, except for the left arm. The elbow region was slightly swollen, especially on the outer side. There was marked tenderness over the external condyle and the head of the radius. The forearm was held flexed at a right angle and pronated. By passive movement, the forearm could be flexed and extended to about one half the normal degree; but all attempts to produce supination were strongly resisted and very painful.

Roentgenograms (Fig. 1) taken November 8 showed a complete separation of the epiphyseal head of the radius. The epiphysis was lying behind the condyle and at right angles to the shaft of the radius. The line of separation was evidently transverse, and there was no sign of any diaphysial fragment attached to the loosened epiphysis.

Operation (November 10).—Under ether anesthesia, a longitudinal incision was made over the external aspect of the elbow. When the joint capsule was opened, the epiphysis of the radius was found lying free in the joint, behind the external condyle and at right angles to the axis of the arm. The epiphysis was picked up with a forceps and replaced within the grasp of the orbicular ligament, which seemed to hold it snugly and firmly. The joint could then be moved freely. The epiphysis remained in position and rotated with the radius. The capsule was closed with catgut, and the skin incision with interrupted waxed silk sutures. The arm was immobilized in flexion by a plaster cast extending from the axilla to the hand.

The wound remained clean. Passive motion was started ten days after the operation. The cast was removed after two weeks and active movement encouraged. A roentgenogram (Fig. 2) made at this time revealed the upper radial epiphysis back in normal position at the head of the bone. When the patient left the hospital, December 10, she had about 50 per cent. of the normal flexion, extension and supination, as well as complete power of pronation.

Course.—This patient could not be traced until two years after her discharge from the hospital. An examination of the arm at that time (Oct. 22, 1922) showed a complete return of all active movements and an absence of any

deformity. A roentgenogram (Fig. 3) showed that the epiphysis on the injured radius had united with the shaft, although the epiphysis of the opposite arm was still ununited.

The patient was examined again one year later (Oct. 23, 1923). There was no deformity or interference with the movement of the arm. A roentgenogram (Fig. 4) showed that the epiphysis of the uninjured radius had now united to the shaft. A comparison of the measurements of the two bones showed that the injured radius was 1 cm. shorter than the radius of the other arm.

From a review of the literature, separation of the upper radial epiphysis seems to be a very rare injury. Most textbooks do not mention this lesion. Von Bergmann [1] states that it is a rare form of injury about which little is known. Kelly [2] and Daughterty [3] state that they have never seen a separation of this epiphysis. Poland [4] has collected seven cases of this injury. In four of them, no details are given; in three others, the diagnosis was made on physical examination alone. The diagnosis was absolute only in the case of Moullin,[5] described thus by Poland:

> A boy, aged 13 years, fell between a team and a platform, tearing the skin and muscles of his arm. A primary amputation was performed above the elbow joint. The specimen in the London Hospital Museum shows the upper radial epiphysis clearly detached at the epiphyseal line, and partly in the grasp of the orbicular ligament. The diaphysis projecting behind is not otherwise injured; but the orbicular ligament is torn. The synovial membrane of the joint retains its connection with the radius.

Broca [6] mentions four cases that he has seen at operation in which the separated epiphysis was found in the elbow joint, but he does not give any details. Stoecklin [7] in a report of twenty-six cases of fracture of the head and neck of the radius had one case of epiphyseal separation. This occurred in a 7-year-old boy, who fell from a sled, striking his forearm against an iron rod and producing a compound fracture of the upper third of the ulna, with separation of the radial epiphysis. The roentgenogram showed the epiphysis and a small attached fragment from the inner side of the diaphysis, lying free in the outer posterior part of the elbow joint. The patient was treated with heat, passive movement and massage. The result was good, except for a slight defect in supination.

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1. Von Bergmann: System of Practical Surgery, New York, Lea Bros. & Co. **3**:195, 1904.
2. Kelley: Surgical Diseases of Children, Ed. 2, New York, E. B. Treat, 1914, p. 1921.
3. Daughterty, L. E.: Minn. Med. **2**:350 (Sept.) 1919.
4. Poland: Traumatic Separation of the Epiphyses, London, Smith, Elder & Co., 1898.
5. Moullin, C.: Path. Tr., 1888, p. 242.
6. Broca: Chirurgie Infantile, Paris, G. Steinheil, 1914, p. 96.
7. Stoecklin: Beitr. z. klin. Chir. **87**:644, 1913.

Because of the rarity of this lesion, it is difficult to get much data from which to draw conclusions.

Cotton [8] and Beck [9] say that these injuries occur in very young children. My patient was 11 years old.

The causative factor in producing this epiphyseal separation was a blow on the flexed elbow, when the child struck the floor in falling. The force was evidently applied to the outer edge of the epiphysis, causing it to flip out of the orbicular ligament and to assume a position

Fig. 1.—The upper epiphysis of the radius dislocated outward and backward, lying at right angles to the shaft.

at a right angle with the head of the radius. Mechanically, it might be likened to the act of raising a box cover by pressure downward and outward on the hinged edge. Such a displacement could only occur when the elbow was flexed, so that the epiphysis, in moving, could get past the capitellum. Willard [10] thinks that this injury may be caused by

8. Cotton: Dislocations and Joint Fractures, Philadelphia, Saunders & Co., 1911.

9. Beck: Fractures, Philadelphia, Saunders & Co., 1900.

10. Willard: Surgery of Childhood, 1910.

a violent jerk on the arm of a child; Beck thinks that holding up or swinging a child by the arm may cause it. When this lesion occurs as part of the picture in crushing injuries about the elbow, it is usually accompanied by other bone injuries, and there is no typical method by which it is produced.

Anatomically, according to Poland:

The osseous nucleus for the head of the radius appears in the center of the cartilaginous upper end, at the sixth year. Ossification is complete about the

Fig. 2.—Appearance after operation, showing the reposition of the epiphysis at the head of the radius.

sixteenth year, and union to the diaphysis takes place about the early part of the seventeenth year or a little later. This epiphysis is remarkable among those of the long bones, because it is the last to ossify and the first to unite with the shaft. Only the upper part of the head of the radius is derived from this epiphysis; the lower part of the head and the neck are ossified from the shaft. The epiphysis is entirely intra-articular. The synovial membrane of the elbow joint extends far beyond the epiphyseal boundary of the head of the radius, completely lining the entire inner surface of the orbicular ligament. It passes off to blend above the epiphysis of the head by a funnel shaped process,

being attached to the radius only by weak areolar tissue. Although of common occurrence, laceration of the synovial membrane is not an absolutely necessary accompaniment of epiphyseal separation, since this synovial sac is so readily detached from the neck of the bone; yet by reason of its extent, it must be especially liable to injury.

Fig. 3.—Appearance two years after operation, showing both arms. The upper radial epiphysis has united with the shaft in the injured arm only.

In the case reported in this article, the epiphysis was completely detached from the bone, lying free in the joint cavity just posterior to the outer side of the shaft. The orbicular ligament was not injured. In other cases, the epiphysis has remained attached to the shaft by a shred of tissue.

Some writers assert that a true separation of this epiphysis never occurs, but that the bone is broken close to the epiphyseal line and the epiphysis with some attached bone is broken off. Broca, from the four cases that he has seen at operation, thinks that usually some small pieces of bone are broken off with the epiphysis. The roentgenograms

Fig. 4.—Appearance three years after injury (patient, aged 14 years). Both upper radial epiphyses are united.

in the case described showed a clean division at the epiphyseal line with no bone fragments, and none could be seen when the epiphysis was carefully examined at operation, before it was replaced.

It would not seem possible to make a definite diagnosis of this injury without a roentgenographic examination, which is only of nega-

tive value in children under 6 years of age. In many cases, the diagnosis can be settled only by an open operation. However, this lesion should abe considered in all injuries about the elbow joint, especially in children, if there is tenderness and painful mobility of the radial head, with muffled crepitus and little or no deformity. The condition must be differentiated from subluxation of the head of the radius, and fracture of the head or neck of that bone, all of which are much more common than epiphyseal separation.

At present, there is no agreement among surgeons as to the treatment of this injury. Some writers have reported good results, after

Fig. 5.—Appearance of patient three years after injury, showing the full range of motion and the absence of deformity.

using conservative measures such as rest, heat, massage and passive motion. Others have employed open operation, with either removal of the epiphysis or replacement of it. The result in the case herein described was entirely satisfactory, and the procedure was so simple that this method is recommended.

The interesting question of the possible interference with the growth of the radius cannot be answered fully by the evidence from this case. It is well known that most of the growth of the radius comes from the lower epiphysis, which shows a center of ossification about the second or third year, and does not unite with the shaft until some time between the twentieth and twenty-fifth year. The upper radial epiphysis in this case was separated from the shaft in the eleventh year. It was replaced

and, two years later, it was found to be united to the shaft (Fig. 3), although its mate on the opposite arm was still ununited. An examination of the arms at this time failed to show any deformity or any shortening of the radius in which the epiphysis had undergone premature union with the shaft. Roentgenograms taken the next year (Oct. 23, 1923) showed that the epiphysis on the unaffected side had united with the shaft (Fig. 4), although the girl was only 14 years old. A measurement of the radius that had been injured revealed 1 cm. of shortening when compared with the radius of the other arm. That this shortening did not produce any deformity or restriction of motion can be readily seen from the photographs taken, December, 1923 (Fig. 5).

In epiphyseal separations that occur at an earlier age, the interference with the growth of the bone from the upper epiphysis would result in greater shortening. Those cases would probably show the deformity of cubitus valgus formation, as mentioned by Seyberth. As this deformity would cause the olecranon to be deflected toward the medial side, the ulnar nerve might be compressed or stretched, with an ulnar palsy resulting in later life.

TREATMENT OF EPIPHYSEAL SEPARATION OF THE LOWER END OF THE RADIUS*

ISADORE ZADEK, M.D.

NEW YORK

The lower radial epiphysis unites at about twenty years. Separation of this epiphysis, therefore, is seen prior to this time. The trauma which produces this injury is identical with that which produces a Colles' fracture in an older individual.

There are several essential differences between the Colles' fracture and separation of the lower radial epiphysis:

(*a*) In fully 50 per cent. of Colles' fractures, the styloid of the ulna is broken. In separation of the epiphysis, the ulna is commonly broken, but generally at a higher level. There is usually no displacement of the ulnar fragment.

(*b*) In Colles' fracture there is commonly radial deviation of the lower fragment, which may be very difficult to correct, and which may produce the end-result of radial deviation of the hand in spite of active attempts to prevent this occurrence. This is probably dependent on crushing of the fine bony structure at the time of fracture. We are not concerned with this lateral displacement in epiphyseal separation of the lower end of the radius.

(*c*) The periosteum is rather loosely attached to the shaft of the long bones, but its attachment to the epiphysis is more firm, so that where the lower radial epiphysis is displaced backward, the stripped-up periosteum remains fixed to it at its dorsal attachment, and later produces a band of bone; whereas, bone production on the volar surface is less rapid. In those cases where the displacement has existed for two weeks or longer, this callus formation presents sufficient obstacle to reduction to prevent replacement of the epiphysis until this band is severed, which means that after this time has elapsed, open operation will be required to effect reduction.

(d) Not uncommonly, a small fragment of bone from the lower end of the diaphysis just proximal to the epiphyseal line is broken off the dorsal part of the shaft and displaced with the epiphysis.

Among the current expressions of opinion on this subject, we find that:

Rose and Carless are authority for the statement that "Union usually occurs by means of bone, and arrest of the longitudinal growth may

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* Presented before the Orthopedic Section of the New York Academy of Medicine, Jan. 18, 1924.

follow, if the parts are not replaced in exact apposition. This is a matter of importance when one of the bones of the leg or forearm is affected, since deformity of the hand or foot results if the injured bone ceases to grow, and the uninjured one continues its development."

Stimson shows a roentgenogram of one epiphyseal separation of the lower end of the radius with but slight displacement, and gives no

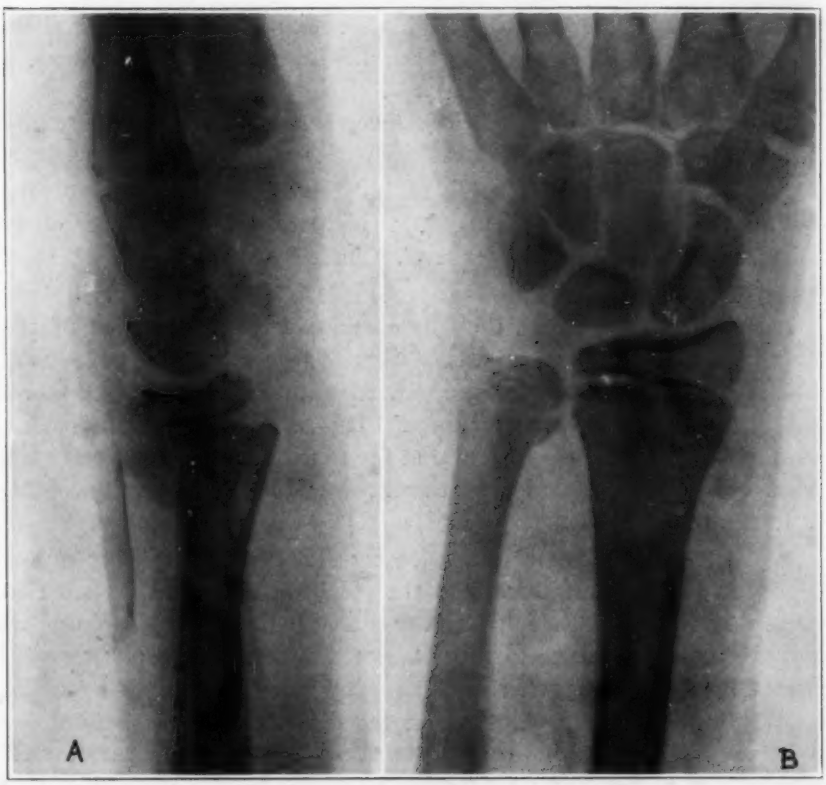

Fig. 1 (Case 1).—Epiphyseal separation, lower end of radius with a fragment of bone broken off the lower end of the radius, and displaced backward with the epiphysis. *A*, lateral view before reduction; *B*, anteroposterior view before reduction, showing that there has been a fracture of the ulna just above the epiphyseal line, but with no displacement.

statement as to its treatment. Moorehead does not even mention epiphyseal separation of the lower end of the radius.

In Davis' "Applied Anatomy," we find the statement:

"The lower radial epiphysis fuses with the shaft at about the twentieth year; therefore epiphyseal separation can occur up to that

time. The epiphyseal line passes across the bone from the base of the styloid process to the upper edge of the radio-ulnar joint.

The displacement, symptoms and treatment are the same as in Colles' fracture, and it is quite possible that many cases diagnosed as Colles' fracture may be epiphyseal separations."

Scudder states: "The treatment of Colles' fracture may present considerable difficulties. Ordinarily, the treatment of a separation of

Fig. 2 (Case 1).—Lateral view of epiphyseal separation, lower end of the radius, with the fragment of bone broken off the lower end of the radius and displaced backward with the epiphysis. After closed reduction.

this epiphysis is simple. There is little difficulty in maintaining the fragments in position in separation of the epiphysis. The epiphyseal separation requires a short time in splints, and there is almost no tendency to reproduction of the deformity after it is once reduced."

Speed states: "That epiphyseal separations (of the lower end of the radius), if replaced, often lead to no permanent interference with growth, but, on the other hand, an unfavorable result may follow."

Dr. Morris K. Smith reported before the New York Surgical Society, April 25, 1923, two cases of epiphyseal separation of the lower end of the right radius. One occurred in a boy aged 13, June, 1921. He was seen at St. Luke's Hospital two weeks after the injury, when he had a marked silver fork deformity. The roentgen ray showed a backward displacement and tilting of the lower radial epiphysis. Attempted reduction under ether anesthesia was entirely

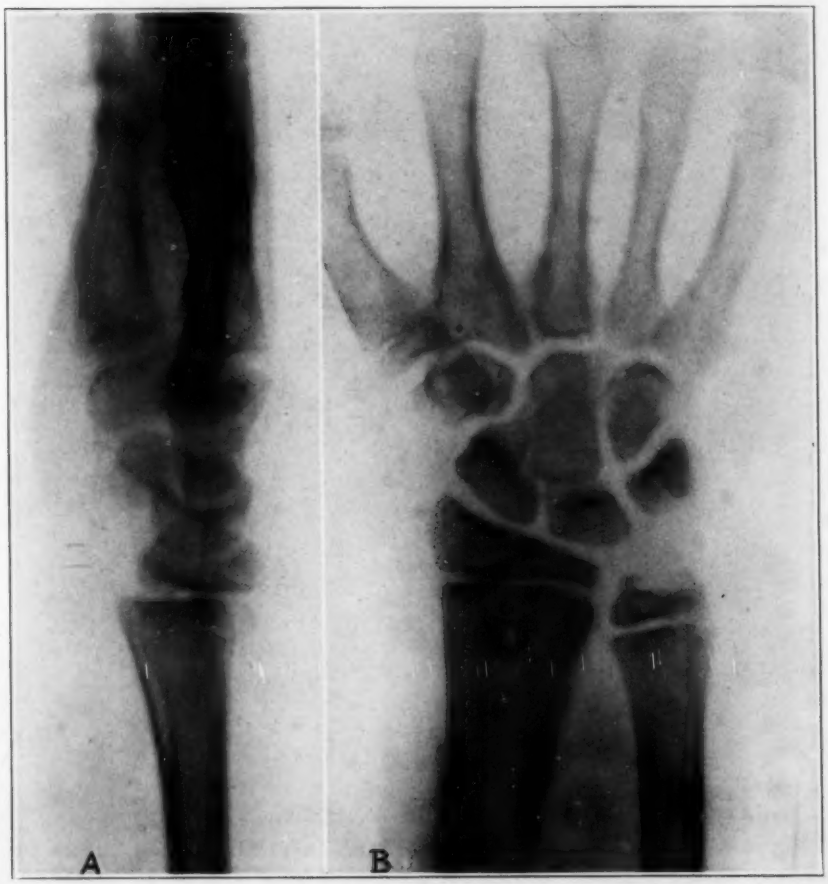

Fig. 3 (Case 2).—Epiphyseal separation, lower end of the left radius, before reduction. A small chip of bone from the lower end of the diaphysis has remained attached to the epiphysis of the radius, and has been displaced with it; apparently the styloid of the ulna is broken but not displaced. *A*, lateral view; *B*, anteroposterior view.

unsuccessful. Nine months later clinical and roentgen-ray examinations revealed the fact that the deformity had disappeared. Today, there is no apparent difference between the two wrists.

Dr. Smith also reported a girl, 10 years of age, who, at the age of 8 years, injured her right hand, August 5, 1921. She was seen in the Out-Patient Department of St. Luke's Hospital, eleven days after the injury. The roentgen ray showed the same condition as above. Attempted reduction under anesthesia was unsuccessful. Five months later, she showed a remarkable improvement and at the present time the wrists, on clinical examination, appear the same, while the roentgen ray has little to show for the old injury.

Fig. 4 (Case 2).—Lateral view of epiphyseal separation, lower end of the left radius, after closed reduction.

It is undoubtedly true that many patients who suffer from the condition under consideration, and who have not had the displacement corrected, ultimately show a wrist which in no essential differs from its fellow. The reconconstructive efforts of nature have achieved a remarkable result! This same result may be seen not infrequently in fractures

of the long bones, yet no one offers this argument as sufficiently valid to warrant making no attempt at reduction. We have no assurance that nature will come to the rescue. It is reasonable to assume that interference with growth is much more likely to follow where a displaced epiphysis is not restored, than where its relationship is normal.

Fig. 5 (Case 3).—Epiphyseal separation, lower end of the left radius with incomplete fracture of the lower end of the ulna, before reduction: *A*, lateral view; *B*, anteroposterior view, showing no displacement.

TREATMENT

There are numerous methods used for the maintenance of reduction after Colles' fracture, and the tendency to dorsal displacement after reduction is probably not great whether the wrist and hand are put in dorsal flexion, in the line of the forearm, or in palmar flexion (which usually means about 10 degrees of palmar flexion and con-

siderable ulnar deviation). The reason for this lies in the fact that, with the fracture, there are two surfaces in contact which present numerous bony spicules "interlocking" after reduction.

On the other hand, in epiphyseal separation there are two smooth surfaces in contact, and for the maintenance of reduction we are dependent, not on any intrinsic bony irregularity of the fractured surfaces, but on some other factor.

Fig. 6 (Case 3).—Lateral view of epiphyseal separation, lower end of the left radius with incomplete fracture at the lower end of the ulna, after attempted closed reduction. The position improved, but the epiphysis is not completely replaced.

With the usual upward and backward displacement of the epiphysis at the lower end of the radius, the epiphysis may be forced into place readily but there is a strong tendency for the displacement immediately to recur. If the hand and wrist are placed in considerable palmar flexion, this recurrence does not take place. As shown by observation

under the fluoroscope, after reduction, the replacement is maintained as long as the hand and wrist are in palmar flexion, but recurs when the hand reaches the plane of the forearm. Roentgenograms of N. D. (Fig. 10) show the change that occurred simply by putting the hand and wrist in slight dorsal flexion after the displacement had been reduced. Reduction can be effected and maintained by placing the wrist and hand, under traction, in palmar flexion of 100 degrees. If

Fig. 7 (Case 3).—Lateral view of epiphyseal separation, lower end of the radius, after open operation, showing anatomical replacement of the displaced epiphysis.

the epiphyseal separation is several days old, it is desirable to force the small fragment into place by digital pressure. In this attitude, the extensor tendons of the wrist and fingers which overlie the epiphysis of the lower end of the radius force the small fragment downward and hold it there. The particular tendons involved are the extensor carpi radialis longus, the extensor carpi radialis brevis, the extensor pollicis

longus and the extensors of the index and middle fingers. The stripped up periosteal flap assists in this and also tends to prevent the fragment slipping forward. This method is simple, direct, and efficient. So far as I know, it has not been previously reported. It is as efficient in maintaining reduction as is the abduction method in fracture of the neck of the femur, or acute flexion in supracondylar fractures of the humerus.

Fig. 8 (Case 4).—Epiphyseal separation, lower end of the left radius, before reduction. There is fracture of the lower end of the ulna, about one inch above its articular border, but with no displacement. *A*, lateral view; *B*, antero-posterior view.

In my small series of cases here reported, the patients were all boys, and in each case it was the left wrist affected.

In order to maintain palmar flexion, I applied a circular plaster extending from the upper forearm to the metacarpophalangeal joints,

Fig. 9 (Case 4).—Lateral view of the epiphysis replaced; the hand and wrist have been forced into right angle palmar flexion with traction on fingers.

Fig. 10 (Case 4).—Lateral view of the hand and wrist pulled into slight dorsal flexion, the epiphysis at the lower end of the radius is again displaced.

leaving the thumb free. The procedure is carried out under anesthesia. It is necessary to make sure that the fingers are free and that the patient can move them readily. This attitude is maintained for two and a half or three weeks. No danger is involved in this attitude if the application has been properly made. When the cast is removed, the hand can be brought to the line of the forearm with but little effort. The arm is carried in a sling for another week.

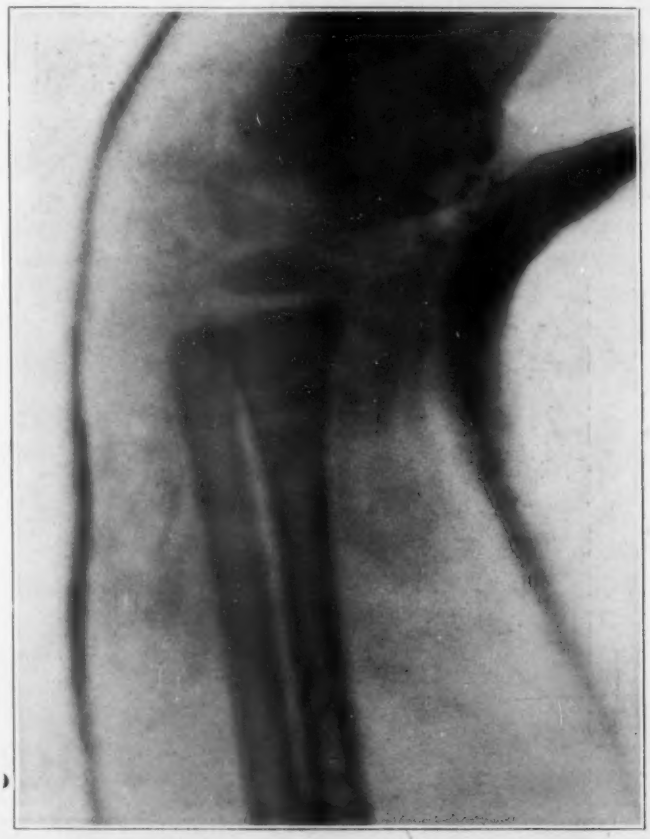

Fig 11 (Case 4).—Lateral view of epiphyseal separation at the lower end of the radius, with the hand and wrist in an attitude of 100 degrees, showing the epiphysis replaced.

REPORT OF CASES

Case 1.—T. O., a boy, aged 13, fell from a tree, Sept. 12, 1922. Epiphyseal separation at the lower end of the left radius occurred. The patient was seen within twenty-four hours after the injury, and a closed reduction was readily accomplished.

Case 2.—F. W., a boy, aged 12, was injured by a fall from a stone wall, Aug. 7, 1923. Epiphyseal separation, at the lower end of left radius occurred.

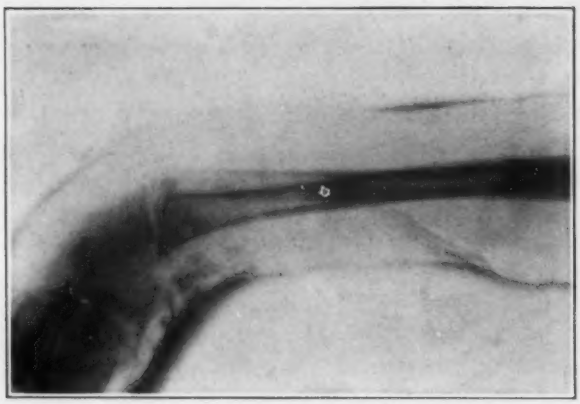

Fig. 12 (Case 5).—Lateral view, showing reduction of epiphyseal separation at the lower end of the left radius, after open operation. Roentgenograms taken prior to the operation were lost, and are therefore unavailable.

Fig. 13.—Attitude after replacement of epiphyseal separation, lower end of the radius, showing outline of the trimmed plaster-of-Paris wrist bandage.

He was seen within twenty-four hours after the injury, and a closed reduction was readily accomplished.

CASE 3.—I. S., a boy, aged 9, received an injury about the middle of August, 1923. He was first seen by me August 28. The diagnosis was epiphyseal separation at the lower end of the left radius. Attempted closed reduction was made August 30. The fact that it was only partially successful was due to the periosteal bridge of bone on the dorsum of the wrist. An open operation was performed September 1. Division of the periosteal band and complete reduction were accomplished.

CASE 4.—N. D., a boy, aged 6, was injured Jan. 8, 1924, as the result of a fall from a porch. The result was epiphyseal separation at the lower end of the left radius. Closed reduction occurred Jan. 12, 1924.

CASE 5.—H. K., a boy, aged 12, received an injury while playing in a building under construction. Epiphyseal separation at the lower end of the left radius took place. The injury had occurred four weeks prior to July 18, 1922, when the patient was first seen by me. Several previous attempts had been made at reduction, all of which had been unsuccessful. An open operation occurred July 21, 1922. Osteotomy was performed at the site of the separation of the epiphysis, and the lower fragment was forced into alinement.

CONCLUSIONS

1. Epiphyseal separations of the lower end of the radius usually remain unreduced when the conventional methods used for Colles' fracture are employed.

2. Often, the ulna is broken with epiphyseal separation of the lower end of the radius, and usually this occurs above the styloid process.

3. In many patients, where the epiphyseal separation has remained unreduced, nature has reconstructed the affected part so that ultimately there is no demonstrable difference between the two extremities.

4. Interference with growth is more likely to occur where the displaced epiphysis has not been replaced.

5. Interference with growth may occur in spite of complete replacement, and the family should be so informed. In the small series given above, the longest time that one of the series has been under observation is a year and a half after the injury. There is no demonstrable difference between the two wrists in any of these patients.

6. By the use of palmar flexion (about 100 degrees), we have a simple, direct and mechanically efficient method of treatment. This reduction should be made under anesthesia and the attitude maintained for two and a half or three weeks. The fingers should be left free and the patient should be able to move them readily though the attitude of palmar flexion makes it impossible for him to make a fist. After the removal of the plaster cast, there is no difficulty in forcing the hand into dorsal flexion.

7. The method of treatment described above has been applied to recent epiphyseal separations requiring only closed reduction. It has

been applied to one open operation where the posterior periosteal band of new bone required division before the fragment could be forced into place, and to one open operation requiring osteotomy, union having become solid with the epiphysis displaced. Reduction was readily effected by placing the hand and wrist in the attitude of palmar flexion after division of the bone at the site of fracture.

8. Open operation should be performed through a lateral incision just anterior to the insertion of the tendon of the brachioradialis into the base of the styloid of the radius, as this will readily expose the line of separation, whereas, if the incision is made on the dorsum, the callus formation may produce a confusing picture.

No anteroposterior roentgen-ray photographs are shown after reduction, as there was no lateral displacement prior to, or subsequent to, reduction in any of these patients.

THE DEPOSITION OF CALCIUM PHOSPHATE AND CALCIUM CARBONATE IN BONE AND IN AREAS OF CALCIFICATION

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In adult bony tissues the matrix in which the bone cells are embedded appears as a clear homogeneous mass, giving no visible indication of the large amounts of calcium carbonate and phosphate which are contained in it, although these salts form two thirds of its mass. The only visible evidence of the presence of these salts is to be found in newly forming, very rapidly growing bone in the fetus, where discrete particles, or separate granules, have been recognized. Adult bony tissues show only homogeneous fused masses.

The organic basis of the matrix consists of fibers formed by the bone cells, similar to those of white fibrous tissue. In bones preformed in cartilage, the cartilage is destroyed at the advancing edge of the bony growth and replaced by these fibers, which, immediately on their formation, begin to show a deposition of calcium salts in the form of very fine, minute granules (Pacchioni,[1] Schäfer,[2] Watt[3]). These granules show only at the extreme advancing edge of the new bone, for, as the deposit increases, the granules fuse to form a solid homogeneous mass without visible structure, right up to the line of formation of the new fibers at the growing periphery.

The fibers forming the organic matrix of the bone are admittedly a product of the bone forming cells. Uniformity of opinion, however, is absent as to the mode of deposition of the calcium salts. The granules might represent either a precipitation product or a secretory one, and three main views are advanced in explanation of the deposition of the salts. These are:

1. The salts are deposited by precipitation in the matrix of a soluble salt of calcium, such as the chlorid, by carbonates and phosphates found in the tissues.

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1. Pacchioni, D.: Untersuchungen uber die normale Ossification des Knorpels, Jahrb. f. Kinderh. **56**:327-340, 1902.

2. Schäfer, E. A.: Quain's Elements of Anatomy, Ed. 11, London and New York, Longmans, Green & Company, 1912, **2**, pt. 1.

3. Watt, J. C.: The Behaviour of Calcium Phosphate and Calcium Carbonate (Bone Salts) Precipitated in Various Media, with Applications to Bone Formation, Biol. Bull. **44**:280-317 (June) 1923.

2. A modified precipitation theory, in which a soluble double salt, calcium carbonophosphate, is carried in the blood and precipitated in the bone by lowered carbon dioxid content in this tissue. The double salt immediately breaks up into calcium carbonate and dicalcium phosphate, the latter being quickly converted into the tricalcium phosphate.

3. The secretion theory explains the presence of the salts as being due to cellular activities. Calcium is taken from the blood and combined with the carbonate radical in the cell, or with the phosphate radical, the latter being derived from the phosphorus compounds contained in the nucleus, either as a normal cell product or as a product of degeneration.

A thorough study of the precipitation of calcium carbonate and calcium phosphate in colloids was undertaken, and fresh bone from the frog, mouse, guinea-pig, cat, dog, man and human fetus was examined to see if any evidence of precipitation was available. The results of this work have been published in full.[4]

The results of this research, briefly summarized, may be stated as follows. It was found that bone salts precipitated in colloids behave in a very definite manner. Calcium phosphate is always amorphous and granular, just as in aqueous solutions. Calcium carbonate, on the other hand, shows a very characteristic change. It has its typical crystalline shape modified or deformed, and it shows a large proportion of the particles composing the precipitate in the form of spherules, rounded bodies and circular disks (Rainey,[5] Harting,[6] Biedermann,[7] Watt [3]). In mixtures of the two salts, each is easily identified in its typical form. Accessory substances present, such as urea, lecithin, and sodium chlorid, found normally in the blood and the tissues, favor precipitation and spherule formation. The hydrogen-ion concentration

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4. Biol. Bull., (June) 1923.

5. Rainey, George: On the Formation of the Skeletons of Animals, and Other Hard Structures Formed in Connection with Living Tissues, Brit. and Foreign Med. Chir. Review **40**:343, 1857; Precise Directions for Making of Artificial Calculi, with Some Observations on Molecular Coalescence, Quart. J. Micr. Science **6**:41-50, 1858; On the Structures and Mode of Formation of the Dental Tissues, According to the Principle of Molecular Coalescence, ibid. **7**: 212-225, 1859; Some Further Experiments and Observations on the Mode of Formation and Coalescence of Carbonate of Lime Globules, and the Development of Shell Tissues, ibid., New Series **1**:23-32, 1861.

6. Harting: On the Artificial Production of Some of the Principal Organic Calcareous Formations, Quart. J. Micr. Science, New Series **12**:118-123, 1872.

7. Biedermann, W.: Ueber die Bedeutung von Krystallization prozessen bei Bildung der Skelette wirbelosser Tiere, namentlisch der Molluskenschalen, Ztschr. f. allg. Physiol. **1**:154-208, 1902; Untersuchungen uber Bau und Entstehung der Molluskenschalen, Jenaische Ztschr. f. Naturwiss. **36**:1-164, 1902.

of the blood and the tissues favors formation of large spherules, so that the carbonate especially can be very easily identified if precipitated. Small deposits of calcium carbonate in a large amount of phosphate may fail to show as spherules, but remain in the form of coarse granules somewhat darker and differing in appearance from those of calcium phosphate. The granules always remain discrete, however, and I have never seen an example of fusion into homogeneous plates or masses such as are found in fully formed bone.

Examination of bone failed to disclose either spherules, crystals or any discrete particles of bone salts except in the rapidly growing end of fetal bones, as described above, where small particles, which quickly fused, were seen. The literature records no results of this kind except in two isolated cases of bone tumors (Pettit,[8] Oliver [9]) where some spherules were found. The conclusions to be drawn from these facts are given below.

Considering the various foregoing theories, the arguments in favor of or against them may now be considered.

PRECIPITATION THEORY

In favor of this theory is its plausibility; against it are a great array of facts. Bone salts do not take the form in the colloidal bony matrix in which they invariably appear in colloids, even in one so nearly related to bone as gelatin. There is a fixed proportion of carbonate to phosphate in bone, carbonate 15 parts, by weight, and phosphate 85 parts, as proved by Wells.[10] Precipitation will not explain this fixed proportion.

There is also no reason why the bone salts should not be formed in the blood before ever reaching the bone, from the reaction of the absorbed calcium chlorid with the blood salts sodium carbonate and phosphate. It might be argued that such insoluble salts of calcium could not then reach the bone, but it is a fact proved by Pauli and Samec [11] that the salts calcium carbonate and phosphate are soluble in an albuminous solution in seven times or more the amount of their

8. Pettit, A.: Sur le Rôle des Calcospherites dans la Calcification a l'Etat Pathologique, Arch. d'Anat. Micr. **1**:107, 1897.

9. Olivier, E.: Cancer gelatineux du Sein avec Corps Calcaires, Beitr. z. Path. Anat. u. z. allg. Path. **17**:640-647, 1895.

10. Wells, H. G.: Pathological Calcification, J. M. Research **14**:491, 1906; Calcification and Ossification, Harvey Lectures, 1910-1911; Calcification and Ossification, Arch. Int. Med. **7**:721 (June) 1911; Chemical Pathology, Ed. 3, W. B. Saunders and Company, Philadelphia and London, 1918.

11. Pauli, W., and Samec, M.: Ueber Loslichkeitsbeeinflussung von Electrolyten durch Eiweisskorper, Biochem. Ztschr. **17**:235-256, 1909.

solubility in water, so that they could be transported in this form in the blood. This, therefore, leads naturally to the next theory.

THE CARBONOPHOSPHATE THEORY

Barillé [12] has given fairly conclusive evidence that there is formed in the blood a salt known as tribasic calcium carbonophosphate ($P_2O_8Ca_2H_2 : 2CO_2[CO_3H]_2Ca$), which is soluble in the blood concentration of carbon dioxid. Wells believes that on coming to bone where the carbon dioxid content is low, this double salt precipitates, breaks up and finally is converted into 15 parts calcium carbonate and 85 parts calcium phosphate; experimental facts have been adduced in support of this view. The strong point of the theory is that the two salts are brought to and laid down in the bone in exactly the right proportions.

Now Wells has shown that calcium salts in bone are in a state of flux, acting as a great alkali or basic reserve, which can be drawn upon if the body needs increased calcium, as in the case of a pregnancy, or if it is losing calcium steadily, as from a pancreatic fistula. This, of course, demands some change in the condition in the bone which will operate to put the salts into solution. Unless they can dissolve directly, which is very unlikely or they would not remain deposited, then we should expect some sort of reversal of the mechanism of deposition; the carbon dioxid content of the bone would rise and the double salts be reconstituted to pass in solution out of the bone. This is a very unlikely change, as the metabolism of the bone will not change sufficiently to raise the carbon dioxid thus, the naturally low content being given as the reason for precipitation.

A second argument against deposition by this modified precipitation reaction is that crystals and spherules of calcium carbonate, or at least granules, might be expected when the double salt breaks up, but they do not appear, although conditions in the bone are at an optimum for their formation.

SECRETORY THEORY

The fine granules, the form in which the bone salts first appear in the rapidly growing osteogenic fibers, might be interpreted as a secretory phenomenon. The carbonate radical has been explained as being derived from the carbon dioxid in the tissue, the phosphate radical from nuclear activity or from phosphorous compounds freed by cellular

12. Barillé, A.: De l'action de l'acide carbonique sous pression sur les phosphates metalliques; combinaison (carbonophosphates) ou dissolution, applications diverses, J. de Pharm. et de Chim. **19**: 14-71, 196, 245, 295, 1904; Rôle des constituants de la dissociation de la carbonophosphate tricalcique dans la genese du tissu osseux et des diverses concretions a base de phosphate et de carbonate de calcium, J. de Pharm. et de Chim. **1**:342, 1910.

degeneration. This explanation does not account for the fixed proportions between the two salts, and it also gives an unsatisfactory origin to the phosphate radical, considering the large amount of the salt present. The secretory view does explain, however, why no precipitation phenomena are to be seen, why the salts appear in fine granules in or on the osteogenic fibers and rapidly fuse into a homogeneous and apparently structureless mass.

It seems to me that the most logical complete explanation of the deposition of the bone salts is therefore to be obtained by combining two of the foregoing views, as follows: Evidence is in favor of the calcium being carried in the blood as the soluble double salt, calcium carbonophosphate. This, I believe, correctly explains the carrying of the salts to the bone, to which it supplies both carbonate and phosphate in exactly the proper proportion. But from this stage onward, evidence is in favor of the view that this salt is taken from the blood and deposited in the bone by the action of the osteoblasts.

This view also provides for a reversibility of the direction of travel of the calcium. The cell may take up the bone salts and pass them back into the blood, a process which is well known and recognized in bone absorption. Grafts of bone, dead or living, used by surgeons in operative repairs of bone (Gallie and Robertson [13]) are invaded by osteoblasts from the healthy surrounding bone, and these cells absorb the graft and replace it by new bony tissue formed by themselves, this process being known as creeping replacement. Moreover, when the body is being robbed of its normal supply of calcium, as it is during pregnancy or in the case of a pancreatic fistula, there is rarefaction of the bones by the taking up of bone salts from them. If osteoblasts are to be given the credit for the removal of bone by "absorption," as most workers in this field have called the process, I see no reason why the reverse process of bone formation by secretion cannot also be credited to them. A further argument in support of this view is that the osteoclasts, the absorbing agents of normal bone, are believed by many to be only modified osteoblasts.

REVERSIBILITY OF THE TRANSPORT OF CALCIUM

These facts also suggest that there is maintained in the body a certain calcium balance similar in its workings to the well known carbohydrate balance. The carbohydrate balance is between the sugar content of the blood, the liver cell, and the liver's reserve store of glycogen. Sugar is removed from the blood by the hepatic cells and deposited as glycogen when the content in the blood is high. The reaction is reversed when

13. Gallie, W. E., and Robertson, D. E.: The Transplantation of Bone, J. A. M. A. **70**:1134-1140 (April 20) 1918; The Repair of Bone, Brit. J. Surg. **7**:211-261, 1919.

the blood is poor in sugar. Similarly, with a normal calcium content in the blood, the osteoblasts can obtain and deposit bone salts, but with blood poor in calcium the reaction will be reversed, salts being removed from the bone to raise the calcium content of the blood toward normal. The calcium in the bones is thus a great alkali reserve in a state of flux, with an interchange of material more frequent than has been formerly supposed, thus bringing the bones more into line with other living tissues. That bone is an active living tissue with cells full of vitality has been shown in many ways, and is being realized more and more, especially by surgeons. The old idea, that bone is an inert mass and that material once deposited in it remained for many years or until that part of the bone was destroyed in growth processes is no longer wholly tenable.

This shows the importance of keeping up a normal calcium supply in the blood in children, and in those suffering from fractures and diseases of the bones; it bears out the clinical observations that foods and medicines rich in calcium and in phosphates aid in proper skeletal development in children, and also in the repair of fractures.

DIFFERENCES IN CALCIFICATION

The foregoing views imply a vital, specific action of the osteoblasts. There is no more reason to doubt this than to doubt the specific action of any other secretory cell. A further indirect proof of this activity may be obtained by attempting a comparison of ossification with calcification. Wells states that calcium salts are deposited in identical proportions in both cases, the salts in a calcified area being exactly the same as in a bone matrix. The difference lies in the matrix, in bone being a regular system of collagenous fibers formed by the osteoblasts, in calcified areas being either old and dense, white, fibrous tissue or areas of necrosis. In all cases, the matrix for the deposit is one of low grade activity, with a small carbon dioxid content, allowing the precipitation of the carbonophosphate which infiltrates the tissue.

This view is correct as far as it goes, but it does not reach far enough. I believe calcium salts are transported as the complex carbonophosphate and so reach the area of deposit in the exact proportion in which they are found. Here, however, differences occur. The bone shows no visible evidences of precipitation. Small pieces of fresh, unaltered bone, examined microscopically by Bast's method,[14] are transparent and homogeneous, and show no discrete particles and no visible structure apart from the bone cells. Areas of calcification show a characteristic deposit which is not homogeneous. Calcified areas in arteries have an appearance as though formed of incompletely fused

14. Bast, T. H.: Studies on the Structure and Multiplication of Bone Cells Facilitated by a New Technique, Am. J. Anat. **29**:139-157 (July) 1921.

masses of granules and sometimes show irregular crystalline masses, and in one calcified pineal gland undoubted calcium carbonate spherules were identified by me in considerable numbers. The bony matrix can be rarefied and its salts removed, but as far as I know there is no evidence of the absorption of calcified areas, but these, once formed, tend to persist. The main difference in the deposition of the salts in the two cases depends on the presence or absence of the osteoblasts.

The first appearance of a deposit of calcium salts in bone is in the form of very fine granules in or on the newly formed fibrous base. The granules quickly fuse to a homogeneous mass. Such a phenomenon may be interpreted either as a secretory or a precipitation process, according to the bias of the observer. In view of all the previously cited facts, I inclined to the view of a secretory origin, the bone cells being the active agent for putting these salts into the matrix.

On the other hand, in calcified areas, it follows, in view of the differences from bone mentioned previously, that Wells is correct in stating that in these cases the phenomenon is a precipitation. The soluble double salt infiltrating a necrotic area, or mass of old white fibrous tissue, enters an area low in carbon dioxid and precipitates. The fact that there are no osteoblasts here to cause removal by cellular activity and that the carbon dioxid content of these areas cannot be easily raised explains the permanence of the deposit, removal not being possible without increased solubility which requires increased carbon dioxid.

SUMMARY

1. Calcium phosphate and calcium carbonate show characteristic easily identified shapes of particles when precipitated in colloids.

2. The bone salts are not present as discrete particles in bone, and, even in rapidly growing parts, show no evidence of being deposited by simple precipitation.

3. Barillé has shown that calcium salts are transported to the bone in the form of a complex double salt, calcium carbonophosphate.

4. Evidence favors the view that the salts in bone are deposited by activity of the osteoblasts, as a secretory phenomenon.

5. The direction of travel of the calcium salts can be reversed. They can be taken from the bone to raise the blood content when it is low. There is evidence of the presence of a calcium balance between bone matrix, osteoblasts and blood similar to the carbohydrate balance between glycogen, liver cell and blood.

6. In calcification, the same salts are present as in ossification and in the same proportion. The difference is that osteoblasts are absent, and instead of a bony matrix there is an area either of fibrosis or necrosis.

7. There is evidence that calcification is a precipitation phenomenon, and in support of this view discrete characteristic spherules of calcium carbonate have been seen in a calcified pineal gland, as well as granules and irregular crystalline masses in calcified areas in the walls of arteries.

8. The presumption is that as its origin is by precipitation a calcified area is permanent and neither will it disappear nor will it show rarefying changes such as may be seen in bone.

EMBOLECTOMY

REPORT OF A CASE *

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The removal of an embolus from an artery by actual incision into the vessel is a relatively recent procedure as well as a rather technically difficult operation. This field of surgery is new, and has developed following the advances made in surgery of the vascular system. The first successful attempt at removal of an embolus by arteriotomy was made by Labey in 1911. Since then, some seventy or eighty cases have been reported in which embolectomy was attempted. Key [1] of Sweden reports ten cases of his own with fifty-one others, which are mostly those of surgeons on the Continent. Buerger [2] of New York reports two cases of his own, and the literature contains references to two other cases.[3]

Emboli usually originate from diseased heart valves but they may also come from the lining of atheromatous vessels and aneurysms. In rare instances, they may originate from tuberculous processes in the lung.[4] Emboli may be single or multiple. The natural place for an embolus to lodge is at the point of bifurcation of the artery, or where a large branch is given off. The vessels most commonly affected, from an operative point of view, are, in order of frequency, the femoral, the aorta at its bifurcation, the brachial, the popliteal and the axillary. Following the lodgment of an embolus in an artery, secondary thrombosis may occur. This may take place within two hours, or it may never appear. With the appearance of secondary thrombosis, the likelihood of the development of gangrene increases because of the occlusion of branches of the vessel and the coincident decrease of collateral circulation.

The symptoms of embolism are more or less familiar to all of us, but because of the importance of early recognition of this condition, I will discuss them briefly. The first symptom is usually pain, the char-

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* Read before the New York State Section meeting of the American College of Surgeons, Albany, N. Y., May 13, 1924.

1. Key, E.: Surg., Gynec. & Obst. **36**:309 (March) 1923.
2. Buerger, L.: Surg., Gynec. & Obst. **36**:463 (April) 1923.
3. Sencert, L., and Blum, P.: Bull. Acad. de méd., Par. **88**:84-87 (July 25) 1922.
4. Personal communication to the author.

acteristics of which are its sudden onset and severity. Almost at the same time, there appears in the affected part a sensation of coldness or numbness. Then the skin begins to grow pale until it may even appear cyanotic. It is cool to the touch. Gradually, motility is lost, first the finer movements disappearing and then the coarser ones. The pulse below the level of the embolism ceases. Occasionally, in thin persons, the embolus can actually be palpated as a nodular segment of the otherwise normal feeling artery.

Thrombosis is the only other condition of an artery that could be easily confused with embolism. The chief points in making a differential diagnosis between these two conditions are the following: In thrombosis, there are usually premonitory symptoms such as cramps, paresthesia, etc.; in embolism, the onset is sudden and painful, coming on without any premonitory signs. In cases of embolism, there is usually a demonstrable source for the embolus such as a diseased endocardium, while in thrombosis there is usually evidence of more or less general vascular disease. Venous thrombosis may be confused with arterial embolism, but it may easily be differentiated by remembering that in the former the affected part is usually warm, cyanotic and swollen while in the later the part is cold, pale and slightly shrunken. Rarely is the pulse absent in venous thrombosis.

The outcome of a given case of embolism depends on the location of the embolus, the presence or absence of other emboli, the length of time elapsing between the onset of symptoms and operation, the extent of damage to the intima of the vessel at the time of operation, and the general condition of the patient. An embolus may be so situated that it is difficult to attack, thus rendering the prognosis in that instance less favorable. The presence of other emboli is another important factor, for often the operator removes what he considers a solitary embolus only to find that there are others beyond. The length of time that elapses between the onset of symptoms and the beginning of operation appears to be very important, but no definite rules can be formulated as yet because of the paucity of reliable statistics. However, a study of the recorded cases certainly proves that operation within from two to twelve hours is much more likely to be successful than when it is delayed longer. As the intima of the vessels is composed of such delicate endothelial cells, the slightest roughening produced by the presence of an embolus or by an operative incision of the wall, may be sufficient to cause further trouble even if the embolus has been satisfactorily removed. The relationship between the general condition of the patient and the operative result differs little in such cases from that existing in general surgical cases.

After all, most of us judge the value of any form of treatment by the results obtained in recorded cases. In no case of embolism where

operation was performed after twenty-four hours was the outcome successful. Key [1] reports a series of thirty-six patients operated on within the twenty-four hour period. Of these, eight died, twelve developed gangrene and sixteen are reported as cured. In this series, there were two cases of embolism at the bifurcation of the aorta in which the patients were operated on with successful outcomes. It was thought that infected emboli should not be attacked, but Buerger [2] reports a case in which he successfully removed an infected embolus from the brachial artery, following an operation for appendicitis. In this case, the symptoms of embolism of the right brachial artery appeared three days after an operation for gangrenous appendicitis. Three hours after the onset of symptoms of embolism, Buerger removed the embolus, but circulation did not return to the occluded vessel. Gangrene did not ensue, however, and, in spite of the development of abscesses and finally a septicemia, the patient recovered the complete use of the affected part. Buerger's other case of embolism followed an amputation of the leg for gangrene. Some six hours after the operation, the patient developed signs of embolism of the right brachial artery and about seven hours later Buerger removed the embolus, after which the circulation immediately reappeared in the vessel below. Unfortunately, this patient developed symptoms of embolism of the vessel of the remaining leg some seven days later and died without an operation. Sencert and Blum [3] report a case of embolism of the axillary artery in a man of 58. A successful removal was followed by a complete relief of symptoms.

The technic of embolectomy demands a thorough knowledge of modern blood vessel surgery and adherence to strict aseptic technic. The embolus is located by determining where the pulsations of the vessel cease, by noting the level of the anesthesia and pallor, and by keeping in mind the location of important branches or bifurcations. The operation is best performed under local anesthesia. Incision into the vessel wall should be made either above or below the site of embolism in order to avoid traumatizing an already irritated area of intima. The whole operative field, and especially the vessel itself must be carefully protected against drying by the use of a saline solution. Following the removal of the embolus, with the assurance that there remains no further obstruction in the vessel, it is sutured. For intimate details of this procedure, I would refer you to any recent publication dealing with vascular surgery. After the operation is complete, it is wise to keep the patient quiet and the parts warm so that nature may be aided in restoring circulation to the damaged area.

The following report is of a case of embolism of the right brachial artery in which the embolus was removed. Gangrene of the arm ensued, followed by the death of the patient.

REPORT OF CASE

History.—J. T., a man, aged 63, a patient at the Tuberculosis Sanatorium, was transferred to the Albany Hospital because of a disturbance of the circulation of his right arm. About 2:30 a. m. on the day of admission, he was awakened by a feeling that his arm and hand were asleep, as though he had been lying on them. Then he noticed that he was gradually losing sensation in the hand and arm. Finally, muscle control of the parts was lost about one-half hour after the onset of first symptoms. At first, the forearm and hand were somewhat blue, but later they became pale and cold to the touch. There was nothing in the previous history of the patient having any bearing on his present complaint. He had been a sufferer from pulmonary tuberculosis for several years.

Examination.—The physical examination of the patient, made at the surgical service about 7 p. m. that night, revealed moderately advanced tuberculosis of both lungs. The heart was considered normal. With the exception of the right arm, all other findings were negative. The right forearm and hand were pale blue in color, and the fingers were held in a state of partial flexion. The hand was decidedly cool to the touch, but bodily heat was felt just above the wrist. The skin was inelastic and showed only a very faint capillary pulse. No arterial pulsation could be distinguished until one went as far up as the axillary. The patient had no voluntary control over motion below the elbow, and tactile sensation was absent to almost this level. No nodules could be felt in the brachial in spite of the thinness of the patient.

Operation.—In view of the certainty of the development of gangrene of the limb, it was decided to attempt removal of the embolus, which was thought to be located in the brachial at the point where the superior profunda is given off. Accordingly, an incision was made down on the vessel beginning at the junction of the axillary and brachial, and the brachial traced down to a point where the pulsations ceased. This was found to correspond to the location where the superior profunda comes off. The vessel was then carefully isolated from all surrounding structures, and clamped off above and below the site of obstruction. Keeping the tissues moist with saline solution, incision was made into the vessel just above the location of the embolus. With a pair of fine forceps this was easily removed. Search was made for other emboli, but none were found. The clamp was then released from the proximal end of the vessel and reapplied as soon as blood was seen to gush from the incision. Then the incision in the vessel wall was carefully sutured with fine silk which was well covered with petrolatum and the clamps removed. No pulsations appeared at the wrist, although pulsations could be traced for a considerable distance below the site of incision in the vessel. As there was no leakage from the sutured vessel, the wound of the soft parts was closed without drainage. The whole arm was then done up in cotton and kept warm by dry heat.

At first it appeared that the circulation in the hand was slightly better in spite of the absence of a palpable pulse at the wrist. With the appearance of pain in the hand, we were greatly encouraged, for previously there had been no sensation at all. However, the condition of the hand gradually became worse until it was evident five days later that gangrene was developing. Further operative procedure was delayed until a definite line of demarcation should appear. About ten days from the time of the first operation, the line of demarcation was definite and so the arm was amputated through the upper third, under local anesthesia. The patient made a very good recovery from the operative

shock, and the wound began to heal nicely. On the third day after this, however, he developed signs of dilatation of the heart which became progressively worse and terminated in death.

Unfortunately, we were not permitted to make a postmortem examination of the deceased. The amputated arm, however, was carefully studied. The vessels of the arm were very carefully dissected, and sections were taken at varying levels for microscopic examination. The oldest thrombus was located in the brachial region where a small vessel was occluded by a thrombus that was being organized. The brachial artery in the cubital region contained a red thrombus, possibly propagated from further up. The radial vessels, which were in a zone of cellulitis, showed thrombosis and acute angiitis. At all levels, the venae comites were occluded by red thrombi.

The possible causes of failure in this case are several. First comes the consideration of the period of time elapsing between the onset of symptoms and operation. This was nearly twenty hours. The importance of the time element has been discussed in detail, so that no further remarks concerning it are necessary here. It is also natural that the intima of a partly collapsed vessel with no circulation through it should easily become thrombosed. There may have been other emboli, distal to the one removed, which were not discovered at the time of operation. Lastly, the lowered resistance of the patient with pulmonary tuberculosis in an active state and a weakened myocardium probably played an important contributing part in bringing about the failure.

SUMMARY

Embolectomy is a rational method of treatment for certain circulatory disturbances.

The diagnosis of embolism is made upon the history of sudden, severe pain along the course of the vessel, accompanied by rapid loss of motion and sensation of the parts with absence of pulse distal to the site of obstruction.

The actual operative treatment demands a knowledge of modern blood vessel surgery and strict adherence to aseptic technic.

The prognosis in a given case depends on the duration of symptoms, the absence of unrecognized emboli, the location of the embolus, trauma to the intima and the general condition of the patient.

28 Eagle Street.

ABNORMAL ARTERIOVENOUS COMMUNICATIONS, ACQUIRED AND CONGENITAL

II. THE ORIGIN AND NATURE OF ARTERIOVENOUS ANEURYSMS, CIRSOID ANEURYSMS AND SIMPLE ANGIOMAS

MONT R. REID, M.D.

CINCINNATI

In the course of my studies of arteriovenous aneurysms the similarity between them and cirsoid aneurysms and simple angiomas was frequently noted. The purpose of this paper is to point out the likeness of these three conditions, and to state my reasons for believing that cirsoid aneurysms and simple angiomas are caused by abnormal arteriovenous communications, and are, therefore, not of the nature of new growths.

ABNORMAL ARTERIOVENOUS COMMUNICATIONS

Scope of the Term.—The capillary bed is the normal communication between the arterial and venous systems. Without discussion, it may be stated that those conditions to which the term arteriovenous aneurysm is generally applied come under the heading of abnormal arteriovenous communications. This conception of an arteriovenous aneurysm has been accepted ever since the condition was accurately described and its cause recognized by William Hunter.[1] In passing, it may be interesting to note that both Antyllus [2] and Albucasis [3] accurately noted the physical signs of a condition which we now know was arteriovenous aneurysm, although they did not recognize its cause and could not, therefore, give to it the name of arteriovenous aneurysm.

Cirsoid aneurysms (pulsating angiomas, aneurysms by anastomosis, racemose aneurysms, etc.) have not, however, been generally so regarded. A glance at the modern textbooks of surgery and pathology shows that this condition is generally considered as a neoplasm. Of this opinion are Matas,[4] MacCallum,[5] Borst,[6] and Delafield and Prudden.[7]

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1. Hunter, William, quoted by Callander: Reports John Hopkins Hosp. **19**:259, 1920.
2. Antyllus: Oribasius **4**:52 (Daremberg edition), cited by Osler in Lancet **1**:949 (May 8) 1915.
3. Albucasis, cited by Osler: Lancet **15**:949 (May 8) 1915.
4. Matas, Rudolph: S. Clin. N. Am. **2**:1165 (Oct.) 1922.
5. MacCallum: Textbook of Pathology, Philadelphia, W. B. Saunders Company, 1920.
6. Borst, Max: Die Lehre von den Geschwulsten, Wiesbaden, F. Bergman, **1**:176, 1902.
7. Delafield and Prudden: Textbook of Pathology, Ed. 8, New York, William Wood & Co., 1907, p. 372.

Ewing [8] speaks of cirsoid aneurysms as partial tumors, Aschoff [9] as arterial angiomas. Adami [10] treats this condition under the heading of aneurysms and makes note of the free anastomoses between the vessels of a cirsoid aneurysm, but does not state if the anastomoses are between arteries and veins. Of the older writers Gross,[11] although he regarded the condition as an arterial tumor, denied the addition of any new blood vessels. He thought that there was simply a dilatation, thinning and elongation of the already existing vessels. Billroth [12] denied that they were tumors, but thought that they were due to an inflammatory process. Wyeth [13] and Erichsen [14] treated them as tumors, and, probably because they pulsated, often confused giant cell sarcomas of the bone with them. Ashurst [15] said that in these tumors not only the arteries but the veins and capillaries were dilated and involved. Most of the authors mentioned agree that the cause of this condition is unknown, and that the tumor (cirsoid aneurysm) is mainly arterial in nature.

That anastomoses between the vessels of a cirsoid aneursym frequently occur has long been known as is indicated by the old name of aneurysm by anastomosis. In the nineteenth century it was under the title of aneurysm by anastomosis that this condition was commonly reported. Yet these anastomoses were most often considered to be between the arteries, and were regarded as a consequence of the disease rather than as its cause.

Although the prevailing idea is that cirsoid aneurysms are neoplastic, there have been many authors who have noted the similarity between cirsoid aneurysms and arteriovenous fistulas, and a few have believed that the same cause explained both conditions, namely, an abnormal communication between the arteries and veins. The development of a pulsating angiomatous condition in the vicinity of a fistula even between

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8. Ewing, James: Neoplastic Diseases, Ed. 2, Philadelphia, W. B. Saunders Company, 1922.

9. Aschoff, L.: Pathologische Anatomie, Jena Gustav Fischer, Ed. 6, **1**:690, 1923.

10. Adami, J. G.: Principles of Pathology, Philadelphia, Lea and Febiger, 1910, **1**:814.

11. Gross, S. D.: System of Surgery, Philadelphia, Henry C. Lea, Ed. 4, **1**:782, 1866.

12. Billroth, T.: General Surgical Pathology and Therapeutics, Trans. by Charles E. Hackley from German Ed. 4, New York, D. Appleton & Co., 1871, p. 529.

13. Wyeth, J. A.: A Textbook on Surgery, Ed. 3, New York, D. Appleton & Co., 1898, p. 260.

14. Erichsen, J. E.: The Science and Art of Surgery, London, Walton and Maberly, 1864, p. 680.

15. Ashurst, John, Jr.: The Principles and Practice of Surgery, Philadelphia, Lea Brothers, Ed. 5, 576, 1889.

large vessels is well known. Stanly,[16] in 1853, suggested that in cirsoid aneurysm the arteries and veins freely communicated. He believed that the condition could only be cured by attacking the center of the aneurysm and thus interrupting this free communication. He knew that the ligation of the main afferent arteries of a cirsoid aneurysm usually resulted in the enlargement of the other smaller arteries. In a careful necropsy study of a remarkable case of cirsoid aneurysm of the head, Wright[17] (1831) proved that the main mass of pulsating vessels was veins, but he did not prove the existence of fistulas between the arteries and veins. Wernher,[18] in 1876, noted that the excision of the center of a cirsoid aneurysm caused most of the large pulsating vessels to cease pulsating, and the dilated arteries to decrease in size or to return to normal. From these observations, he concluded that they were similar to arteriovenous aneurysms. Thorndike[19] (1878) reported a cirsoid aneurysm of the arm as an arteriovenous aneurysm. Cahen[20] (1890), in a case of cirsoid aneursym of the hand, proved a free communication between the arteries and veins and assigned this as the cause of the condition. Bramann[21] classes cirsoid aneurysms as arteriovenous aneurysms. J. M. Warren[22] (1857) while amputating an arm for an unusual varicose aneurysm, observed that the veins carried arterial blood, and a study of the specimen subsequently showed that the veins anastomosed freely with the arteries. In Meleney's[23] (1923) description of the pathology of cirsoid aneuryms ("tumor"), there is a strong suggestion that the arteriovenous communications may be the etiologic factor. James Berry[24] (1906), in discussing a case of a large arteriovenous aneurysm of the neck, makes this interesting comment:

> The very strong resemblance between this case and the much more common ones of so-called cirsoid aneurysm of the scalp and face raises the interesting question whether these latter tumors really consist of dilated and tortuous arteries as is commonly supposed. Personally, I am inclined to agree with those who believe that cirsoid aneurysms really consist of dilated and tortuous veins rather than arteries. It is well known that cirsoid aneurysm of the scalp commonly develops after an injury. It seems reasonable to believe that an injury involving both artery and vein would readily allow arterial pressure to

16. Stanley: M. Times & Gaz. (New Series) **7**:244, 1853.
17. Wright, T. H.: Am. J. M. Sc. **9**:90, 1831.
18. Wernher: Berl. klin. Wchnschr. **13**:165 (March 27) 1876.
19. Thorndike: Boston M. & S. J. **99**:475, 1878.
20. Cahen: Deutsch. med. Wchnschr. **16**:199, 1889-1890.
21. Bramann: Arch. f. klin. Chir. **33**:1, 1886.
22. Warren, J. M.: Boston M. & S. J. **57**:528, 1858.
23. Meleney, F. L.: Surg., Gynec. & Obst. **36**:547 (April) 1923.
24. Berry, James: Lancet **2**:1714, 1906. Ribbert, cited by Ewing: Neoplastic Diseases, Ed. 2, p. 226, Philadelphia, W. B. Saunders Company, and in Mac Callum's Pathology, Ed. 2, p. 968.

be transmitted to the interior of the vein. The increased pressure would naturally cause distention of the thin-walled veins and a tumor composed of dilated and tortuous veins would be formed, just as in the case I have recorded. It has always been difficult for me to accept the common statement that a cirsoid aneurysm is composed of a mass of dilated and tortuous arteries. The point seems to me to be well worthy of discussion.

In addition to the observations of others reported in the preceding paragraph, the reader is referred to Cases 27, 29, 30 and 31 (Paper 1), where, in cases of cirsoid aneurysm, I was able to demonstrate the existence of free communications between the arteries and veins. Case 29

Fig. 1 (Case 29, Paper 1).—A cirsoid aneurysm involving the neck and face, reported by Halsted as a congenital arteriovenous fistula: left, the patient just prior to the second operation; right, four years after the excision of a large arteriovenous communication. There were several large communications between the branches of the external carotid artery and the neighboring veins. She was completely relieved, but there are still evidences of a small fistula in the region of the parotid gland.

was reported by Halsted [25] as an example of a congenital arteriovenous fistula. Later, without changing his mind as to the etiologic factor, he felt that the condition of this patient was like that of a cirsoid aneurysm. In Cases 30 and 31, it was observed that the veins were filled with

25. Halsted, W. S.: Tr. Am. Surg. A. **37**:262, 1919.

arterial blood and the communications between the arteries and veins were found. The anastomoses in Case 27 were demonstrated by injections. In connection with Case 30, it is interesting to note what M. M. Carnel and Ranvier say about an angioma of the bone:

> The tissue is hollowed out into alveoli, communicating in a very irregular manner with each other, very much in the way as do the alveoli of carcinoma. The blood circulates in this cavernous system, which occupies the place of the capillary system, situated as it is between the arteries and veins. The circulation through these cavities is very active.

Cirsoid aneurysms and arteriovenous aneurysms are alike in many other respects. Etiologically, trauma and congenital abnormalities are productive of both conditions. Trauma is by far the most frequent cause of arteriovenous aneurysms; it probably is the most frequent cause of cirsoid aneurysms. Many of them have followed a blow on the head, and most of the cirsoid aneurysms occur in this region. In this very vascular region where the bone is near the surface, blows might easily establish an arteriovenous communication taking the form of a cirsoid aneurysm. Indeed, many of the so-called congenital cirsoids of the head may have had their origin in the pressure exerted on the skull at childbirth. Clinically, both conditions lead to enormous dilatations and pulsation of the involved veins and proximal arteries. Therapeutically, each condition may be cured by obliterating in some way the abnormal arteriovenous communications, and neither can often be cured in any other way.

From a study of the reported cases of cirsoid aneurysm and of my own cases, I cannot escape the conclusion that there is no difference between this condition and arteriovenous aneurysm, except that cirsoid aneurysm has been applied to that condition which results where abnormal arteriovenous communications occur in the more peripheral and smaller vessels.

The histogenesis of simple angiomas is not yet definitely agreed on. Most all authors of textbooks on pathology mention the controversy that has existed for a long time over the advisability of calling simple angiomas true tumors. Everyone agrees that the vascular endothelium may give rise to tumors possessing the properties of independent growth and even of metastases. Examples of such growths are the hemangioendotheliomas, pigmented nevi, and the hemangioma simplex described by Borrman.[26] Yet the great majority of so-called angiomas are composed simply of swollen blood vessels and do not exhibit the qualities of independent growth characteristic of true neoplasms. For this

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26. Borrman: Beitr. z. path. Anat. u. z. allg. Path. Ed. 40, p. 372, cited in Ewing's Neoplastic Diseases, Ed. 2, Philadelphia, W. B. Saunders Company, p. 226.

class of angiomas Albrecht,[27] who considered them to be due to developmental defects, suggested the term of hemartoma. A strong opponent of the neoplastic nature of angiomas is Adami.[10] Thoma [28] considered mechanical factors a very important influence in the growth of angiomas. Others (Rokitansky [29] and Borst [6]) regarded many of them as a simple hypertrophy of vascular segments without neoplastic overgrowth. Unna,[30] perhaps noting the frequency of simple angiomas in certain locations of the body, suggested that they were due to an abnormal pressure exerted during fetal life. Others (Ewing,[8] MacCallum,[5] Aschoff,[9] etc.), while stating the controversy over the histogenesis of angiomas, are inclined to treat them as neoplasms or partial neoplasms arising from a displaced segment of the vascular bed which comes to possess a limited power of an aberrant growth.

Although my researches do not yet furnish definite proof of the etiology of simple angiomas, I cannot escape the conclusion that they are dilatations of the small arteries and veins caused by a traumatic or congenital abnormal communication between the smallest arteries and veins. They are, I believe, arteriovenous communications (without the medium of capillaries) between the arterioles and venules. On a small scale, they possess many points of similarity to both arteriovenous and cirsoid aneurysms. The free abnormal arteriovenous communications in the latter two usually lead to a widespread enlargement and dilatation of the neighboring arteries and veins, differing from angiomas only in their pulsatile nature and rapid enlargement. Angiomas, too, may grow, become more susceptible to such strains as that of crying or of pregnancy, begin to pulsate, develop free anastomoses between arteries and veins, and soon exhibit all the clinical characteristics of a true cirsoid aneurysm. Angiomas are the common seats of origin of cirsoid aneurysms. If angiomas are the result of either congenital or acquired abnormal arteriovenous anastomoses, it becomes not a little surprising, when we consider the terminal vessels involved and their low blood pressures, that a balanced adjustment should occur and many remain as circumscribed stationary lesions, that many should progress and disappear, and that some should grow and assume the proportion of a danger-

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27. Albrecht: Verhandl. d. deutsch. path. Gesellsch. **7**:153, 1904, cited in Ewing's Neoplastic Diseases, Ed. 2, Philadelphia, W. B. Saunders Company, 1922, p. 230.

28. Thoma, R.: Textbook of General Pathology and Pathological Anatomy, Trans. by Alexander Bruce, London, Adam and Charles Black, 1896, p. 555.

29. Rokitansky, cited by Ewing, James: Neoplastic Diseases, Philadelphia, W. B. Saunders Company, p. 226.

30. Unna, cited in Ewing's Neoplastic Diseases, p. 226.

ous cirsoid aneurysm. The fate of angiomas is probably determined by the freeness of their arteriovenous anastomoses and the strains to which they are subjected.

Many persons have observed on themselves the frequent appearance and disappearance of small telangiectases or nevi. Minute senile

Fig. 2.—A large angioma of the leg in a man aged 49. It developed in a birthmark and grew gradually. There was no thrill or bruit. The veins, however, contained arterial blood. The connection between this angioma and the arterial system was by means of rather large arteries coming directly through the cortex of the bone.

angiomas are well known. Even very large angiomas, either spontaneously or as a result of inflammation, thrombosis or slight surgical inter-

vention, may disappear. In my experience an extensive angioma involving the entire leg was cured, by thrombosis, after the excision of a very small portion of it. McLeod [31] had a similar experience with an angioma of the arm, and there have been many other such observations. W. W. Keen [32] reported two cases of pulsating angioma of the hand and foot, following trauma. Angiomas may result from the extraction of a tooth, and they frequently occur on the mucous membrane of the cheeks and on the lips. Other characteristics of angiomas which are equally uncharacteristic of tumors could be mentioned. Those mentioned speak strongly for a traumatic establishment of an abnormal communication between the arteries and veins. In the light of the work by Sylvester,[33] Sabin [34] and Woollard,[35] the congenital lesions become easily understood.

It seems to me that Ribbert's excellent work on the origin and growth of simple angiomas rather supports my conception of their origin. "By means of interstitial injection he finds that the vessels have few or no lateral anastomoses, while the injection mass passes freely into the efferent artery and afferent veins but not into the tissues surrounding the tumor." [8] Such results are what one would expect if, without the medium of a capillary bed, the terminal arteries and veins anastomosed. On the other hand, such results would hardly be expected in a true new growth. Virchow [36] made the important observation that the cavernous hemangiomas of the liver could be injected through the main portal or hepatic veins or arteries. He believed that these hemangiomas of the liver might spontaneously disappear leaving scars. Thomas H. Wright [17] (1831), following his studies of a cirsoid of the scalp, made the statement that "something analogous obtains in nevi materni; the action of the small vessels of which these tumors are composed could not be discriminated by touch in their normal state, yet by some enlargement and free communication in common receptacles or cells, pulsation becomes strongly revealed." Wernher [18] speaks of the absence of capillaries in angiomas and mentions the fact that some grow.

I realize that what I have said in the foregoing paragraphs does not constitute ample proof of my contention that the simple angiomas, cirsoid aneurysms and arteriovenous aneurysms have the same etiologic basis, namely, that they are due to abnormal arteriovenous communications. Further similarities will be cited in succeeding sections in connection with other phases of the subject. It is hoped that research

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31. McLeod, K.: Lancet **2**:1067, 1888.
32. Keen, W. W.: Ann. Surg. **22**:393, 1895.
33. Sylvester: Am. J. Anat. **12**:447, 1911-1912.
34. Sabin, F.: Reports Johns Hopkins Hosp., Monographs, New Series, 1913, No. 5.
35. Woollard: Contributions to Embryology **14**:139, 1922.
36. Virchow, cited in Ewing's Neoplastic Diseases, p. 226.

work on angiomas will soon permit me to offer more convincing proof. The reader is again reminded that there are true vascular tumors, some of which may metastasize, such as the endotheliomas, but that they should not be grouped with the simple angiomas.

Origin of Abnormal Arteriovenous Communications.—These are either acquired or congenital. Nearly all arteriovenous aneurysms are traumatic in origin. Penetrating wounds comprise the main cause. Fractures, amputations and contussions are occasionally productive of arteriovenous aneurysms. Contusion is of particular interest to me as a cause of arteriovenous aneurysm. Rarely does it produce a fistula between large arteries and veins, but I believe that this form of injury is the commonest cause of cirsoid aneurysms, because fistulas are established between the smaller arteries and veins. A. Colles[37] (1855) reported a case of arteriovenous aneurysm between the femoral vessels, caused by a blow which did not pierce the skin. Although trauma is the main cause, a fairly large number of cases of spontaneous origin have been reported in the literature (Pepper,[38] C. Hodlmoser,[39] Kaufman,[40] Humphrey,[41] Barwell, Boinet, etc.). Most of these have been caused by the rupture of an aneurysm into an adjoining vessel, and have occurred between the aorta and the vena cava, the pulmonary artery or the heart. In smaller vessels, abscesses in the walls of an artery have, by erosion, led to spontaneous arteriovenous aneurysms. A remarkable case of such a nature was reported by Riehm; a case of spontaneous bilateral pulsating exophthalmos, following influenza.

The occurrence of congenital arteriovenous aneurysms has rarely been reported. They do, however, occur. One of the earliest cases, although it was not substantiated by necropsy or at operation, follows, as it was reported by Mr. Prescott Hewett.[42]

REPORT OF CASE

History.—Sarah R., aged 17, was admitted to the hospital Feb. 7, 1865. Her mother stated that when the patient was born the right thigh was noticed to be larger than the left, and that the veins of this extremity were enlarged. The girl herself stated that as long as she could remember there had been a peculiar "beating" in the leg. At first the swelling was confined to the thigh, but it soon extended to the leg, and finally to the foot. It caused her little inconvenience unless she walked some distance or stood for a long time, and then the veins became much bigger. Latterly, however, some of the veins near

37. Colles, A.: Dublin Quart. M. J. **20**:341, 1855.

38. Pepper, William: Am. J. M. Sc., New Series, **100**:329, 1890. Riehm, Herman: Deutsch. med. Wchnschr. **48**:287 (March 3) 1922.

39. Hodlmoser, C.: Ztschr. f. klin. Med. **42-43**:251, 1901.

40. Kaufman, Rudolph: Wien. klin. Wchnschr. **18**:1004, 1905.

41. Humphrey, Laurence: Brit. M. J. **2**:1046, 1910.

42. Hewett, Prescott: Lancet **1**:146, 1867.

the ankle had given way and had bleed profusely several times, and it was for this that she sought admission to the hospital. Her mother also stated that she had always been a delicate child, and as an infant had suffered from hydrocephalus.

On admission, the right lower extremity was found to be much enlarged, being not only increased in circumference, but at least 2 inches (5 c.c.) longer than the left. The superficial veins were much dilated, and stood out in the form of large convoluted and tortuous cords under the skin; they were quite soft and could easily be emptied of their contents, and there was no pulsation in them. The femoral vein could also be felt to be much enlarged in the groin, and in it could be perceived a distinct vibratory thrill, which could be traced up to the junction of the two iliac veins in the vena cava, but no thrill could be felt in the latter vessel. A very loud, continuous blowing sound could be traced up the vein to the same spot. She seemed a weak, anemic girl, with an overhanging forehead. There was a loud systolic murmur at the apex of the heart. On the lower part of the outer side of the leg was a large scab, from which the bleeding came.

A few days after admission harelip pins were placed under all the veins that could be seen running in the direction of the point of hemorrhage, and the vessels were then compressed by a twisted suture placed over the needles. The needles were allowed to remain in twenty-eight days. They caused very little irritation, but gradually produced consolidation in the veins.

She was subsequently discharged, very much in the same state as when admitted, the thrill and bruit remaining just the same.

The symptoms in this case render it probable that a communication existed somewhere between the arterial and venous circulation, while the fact that the thrill and bruit terminated abruptly at a spot where a large artery and vein are in close relation, namely, where the common iliac artery (on the right side) lies upon and crosses the common iliac vein, appears to point to this spot as the place of communication. That the opening was congenital seems also probable, as the enlargement of the thigh and the dilated state of the veins were noticed at birth and there was no probability of disease having thinned the coats or of an accident to such deep structures. Moreover, the fact that she suffered from hydrocephalus proves that there was an unhealthy state of system, which may, and possibly would, have retarded development.

Two other cases have been reported by Busche[43] and Halsted.[25] Halsted's case, however, presented the clinical picture of a cirsoid aneurysm or a pulsating angioma. Of the congenital cases reported in this paper, one can be called an arteriovenous aneurysm. Case 30 (Paper 1) exhibited a large fistula between the subclavian vessels. The reader is referred to these cases not because there is any essential difference between them and the fairly common congenital cirsoid aneurysms, but because the abnormal communications have happened to occur between large vessels, and the resultant conditions could therefore be called clinically arteriovenous aneurysms.

That cirsoid aneurysms may result from trauma has long been known. Many such cases have been reported (Brodie,[44] Wardrop,

43. Busche, G.: Lancet **2**:413, 1827.
44. Brodie, B. C.: Tr. Med. Chir. Soc. **15**:177 (Part 1) 1929

Meyer,[45] Mynter,[46] Hill,[47] Forbes,[48] and others) and the traumatic origin of this condition is recognized and so stated in some of our modern textbooks of surgery and pathology. Billroth's statement about this condition is interesting: "These aneurysms not infrequently develop after blows; they are most frequent at points where numerous small arteries anastomose, as in the scalp, over the occiput, vertex and temples." An abstract of Sir B. C. Brodie's case, reported in 1829, is given here as an example of the traumatic origin of cirsoid aneurysms.

Miss ———, in the year 1809, being then about 5 years of age, received a severe blow on the forehead, in consequence of her having run against the corner of a bed post. Soon afterwards a small pulsating tumor, not larger than a pea, was observed on the part on which the blow was inflicted. For many years the tumor remained nearly stationary, and as it produced no inconvenience, it excited but little attention. In the year 1821 it had manifestly increased in size, in consequence of which a surgeon in London was consulted, who attempted to cure the disease by pressure. For this purpose compresses were applied over the tumor, secured by a tight bandage round the head. Under this treatment the patient suffered from a constant pain, and so far was it from being of any service, that as soon as the pressure was left off, the tumor seemed to grow more rapidly, and the pulsation in it became stronger than before. From this time also there were frequent attacks of intense headache, which were to be relieved only by blood letting.

After this no local treatment was resorted to until the year 1824, when the tumor, having increased to a still larger size, another attempt to restrain its growth by pressure was instituted under the direction of Sir Astley Cooper, but with no more favorable result than formerly.

In the end of June, 1826, the disease having made still further progress, Sir Astley Cooper was again consulted, and by him a ligature was applied (at four different times) round each of the four principal arteries by which the tumor was supplied. The result of these operations was a slight diminution in size of the tumor and some relief from pain, but even this favorable change was of short duration. In the course of the winter of 1827 the tumor again grew larger and the painful sensations returned with redoubled violence, attended with a constant sense of weight over the eyes and excessive depression of spirits. Occasionally there were paroxysms of pain still more violent than what was usually experienced and followed by a state of extreme languor and exhaustion.

Miss ——— remained precisely in this state, except that the tumor continued slowly to enlarge, until Oct. 9, 1828, when she arrived in London after an absence of many months, and I saw her in consultation with Dr. Robertson, of Northampton. The tumor was now bigger than a large double walnut, occupying a spot on the right side of the forehead, immediately below the margin of the hairy scalp. When the fingers were applied to it, they received an impression as if it was composed of a mass of tortuous vessels, and a strong

45. Meyer: New York M. J. **56**:214, 1892.
46. Mynter, Herman: Ann. Surg. **11**:93, 1890.
47. Hill, J. D.: Lancet **2**:430, 1870.
48. Forbes, W. S.: M. News, London, **66**:663, 1895.

pulsation was perceptible in every part of it. The skin covering the tumor was thin, and on some occasions, as in coughing, when the vessels were usually distended, it appeared as if on the point of bursting. When the scalp was shaved, large and tortuous arteries were to be seen, even from a considerable distance, passing into the basis of the tumor, in every direction, from each temple, from the orbit of the right eye, and over the crown of the head from the occiput. Pressure being made on the two temporal arteries at the same instant, the pulsation of the tumor was perceptible but not greatly diminished. There was a constant sense of weight and pain in the forehead, and the latter was very much aggravated by pressure on the tumor, especially on a particular spot towards its upper edge.

A long steel needle, the length of which was about double the diameter of the tumor, was passed between it and the periosteum, penetrating the skin on

Fig. 3. (Case 27, Paper 1).—A rapidly developing cirsoid aneurysm of the scalp, seven months after a kick received in a football game.

each side. By means of this needle the tumor was raised as much as possible, and a second needle was introduced in the same manner, but beneath and at right angles to the first. A very strong silk ligature was then bound several times around the base of the tumor below the needles, as tight as it could be drawn. The tumor immediately assumed a purple color, as if in a state of strangulation. The operation occasioned great pain both at the time and afterwards, but from the instant of the ligature having been applied, the peculiar sufferings occasioned by the disease were at an end.

Cirsoid aneurysms, however, occasionally occur in parts of the body other than in the head. In a few cases, the hand has been the seat of the trouble and the condition has been ascribed to the playing of baseball

or some other form of injury to the palm. In Samuel Young's [49] case, a blow below the knee resulted in a cirsoid aneurysm. Cirsoid aneurysms most commonly develop in angiomas. But, even then, trauma or strain are frequently the causes that start an otherwise benign and stationary lesion on the road to the development of a serious condition. Following a blow or irritation, the strain of crying or pregnancy, an angioma may grow, pulsate and develop the thrills and bruits characteristic of a large abnormal arteriovenous communication.

The congenital origin of cirsoid aneurysms is well recognized, for children are born with them. Although this is true, it may not be fair to assume that the condition is always due to developmental defects. The possible pressures during intra-uterine life and during the birth of the child may be important etiologic factors. Not a few cirsoid aneurysms have been known to occur at the sites of hematomas caused by labor.

Most simple angiomas are congenital. That some are acquired is undoubtedly true. Keen [32] reports two cases that were the result of trauma; one was on the hand, the other on the foot. Lowenthal (Ewing [8]) reports others. The occurrence of angiomas soon after birth suggests that the trauma at the time of birth may have caused them. Unna believes that intra-uterine pressure is the main cause of congenital nevus venosus.

Of the cases of abnormal arteriovenous communications reported in Paper 1, twenty-seven were of acquired and five of congenital origin. No cases of simple angiomas are included among those reported.

Explanation for Occurrence.—The development of arteries and veins out of a common capillary plexus affords us an explanation for the occurrence of abnormal congenital arteriovenous communications. Halsted drew attention to this fact in his paper on congenital arteriovenous fistulas in which he quotes Sabin. The wonder is that direct congenital communications between arteries and veins do not more frequently occur, when we consider the common bed for their development and the enormous destructive as well as constructive changes these vessels undergo before the final pattern is reached. It is interesting to note that "a vessel may serve for a time as a vein in the return of blood to the heart and may subsequently receive new arterial connections and become an arterial plexus, with the direction of flow of blood entirely changed. Such a vessel is the so-called vena capitis medialis." [34] The direct growth of veins from an artery, such as the cardinal veins from the wall of the aorta, would afford an excellent chance for the persistence of free communications between the two systems. Woollard, in his studies on the development of the principal

49. Young, Samuel: Lancet **2**:824, 1840-1841.

arterial stems in the forelimb of the pig, seems to show very free communications between the subclavian artery and vein in the embryo. With the exception of the foramen ovale and the ductus arteriosus, the persistence of free communications between large arteries and veins is very rare. Case 30 (Paper 1) perhaps offers the most striking example of such an occurrence. Many of the angiomas and cirsoid aneurysms represent congenital abnormal communications between the smaller arteries and veins, and their ultimate fate is determined by the size of these communications and the pressures to which they are subjected. It is even conceivable that large lakes of blood might be caught between two capillary beds, such as seems to be the case in some of our venous angiomas and port wine birthmarks.

CONCLUSIONS

1. Arteriovenous aneurysms and cirsoid aneurysms are caused by abnormal communications between the arteries and veins. Simple angiomas are probably the result of the same cause, and their fate is, perhaps, determined by the freeness of these abnormal communications.

2. Abnormal arteriovenous communications may be congenital or acquired.

3. The embryologic development of blood vessels makes it easier to understand the congenital lesions.

TWENTY-SIXTH REPORT OF PROGRESS IN ORTHOPEDIC SURGERY*

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CONGENITAL CONDITIONS

Cervical Ribs in Children.—Southam and Bythell[1] have studied 2,000 roentgenograms of children at the Royal Manchester Children's Hospital, and found in this collection only nine cases of cervical ribs. These were bilateral in all except one case. In their own experience, they have observed four cases, making a total of thirteen cases in all. Ten of these were in females. Their conclusions are that cervical ribs are congenital abnormalities. In the thirteen recorded cases, twelve were bilateral and ten occurred in girls. Roentgen-ray examination is the only method of revealing the condition. Symptoms from cervical ribs do not appear until adult life is reached. The delay in the onset of symptoms may be due to ossification of the rib, which is not complete until about the twenty-fifth year. In young children, however, cervical rib may rarely give rise to definite symptoms in the upper arm, simulating the symptoms seen in adults. In some cases, the presence of cervical ribs may lead to a confusion in diagnosis with spinal caries and congenital torticollis. The roentgen-ray examination establishes the diagnosis. Only rarely is operative treatment in cervical rib considered necessary by the authors.

Dorsalization of the Seventh Cervical Rib and Hypertrophy of the Transverse Processes.—Mouchet[2] reports a case in which there was dorsalization of the seventh cervical rib and hypertrophy of the transverse processes. This deformity was bilateral and occurred in a child 11 years of age.

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* This report of progress is based on a review of 413 articles selected from 593 titles dealing with orthopedic surgery, appearing in medical literature between Aug. 9 and Dec. 6, 1924. Only those papers which seem to represent progress have been selected for note and comment.

1. Southam, A. H., and Bythell, W. J. S.: Brit. M. J. **2**:844 (Nov. 8) 1924.
2. Mouchet, Albert: Bull. et mém. Soc. nat. de chir. **50**:953 (Nov. 1) 1924.

Case of Dorsalization of the Seventh Cervical Vertebra with a Cervical Rib.—Foucault [3] reports a case of dorsalization of the seventh cervical vertebra occurring with a cervical rib, the patient being 52 years old. An operation was performed for a uterine fibroid tumor, and the day after the operation there were abnormal sensations and swelling in the right arm. Above the clavicle, there was fulness which was tender to pressure. Roentgen-ray examination revealed a bilateral deformity of the seventh cervical vertebra. Circulation was disturbed in the forearm also. The author believes that the condition was probably caused by the use of an apparatus for holding the shoulders during the operation for uterine fibroid tumor, which gave a temporary brachial paralysis.

Experience and Results with the Treatment of the Congenital Dislocation of the Femur in Lange's Clinic in Munich.—Schultz,[4] reporting from the Lange Clinic in Munich on methods of treatment in congenital dislocation of the hip, gives the results in 221 cases, 140 of which were single, and eighty-one of which were double, a total of 349 joints treated during the last ten years. The method of Lange consists in traction similar to Bradford's method, and fixation in extension with moderate abduction and inward rotation. Lange uses two periods of fixation, in all five months, and applies an apparatus of celluloid for after-care. The conclusions made on this series are that the method is not more dangerous than the manual method, but by it the resistance of the tissues is more easily overcome. Of the 349 joints, 90 per cent. gave good results, and 70 per cent. gave ideal results. After-care is of great importance and should be carried on for two or three years, the patient wearing an apparatus for the day and one for the night, and doing exercises for development every day.

Spontaneous Cure of Congenital Luxation of the Hip.—Ducroquet [5] reports two cases of spontaneous reduction of congenital dislocation of the hip, and gives a result of his review of the literature on this subject. He has disregarded all cases but those in which the diagnosis, both of the dislocation and of the reduction, was verified by roentgen-ray examination. He has compiled eleven authentic cases, including two of his own in which the hips spontaneously were reduced. He gives careful histories and tracings of the roentgenograms. Of the two cases reported by the author, one was that of a child of 21 months, who was seen in 1920. The roentgenogram showed a dislocation of the right hip. Additional roentgenograms were made later in 1920 and early in 1921. Both showed the same condition. The child was not seen again until two years later. There was no limp, nor any clinical evidence of dislo-

3. Foucault, Paul: Bull. et mém. Soc. nat. de chir. **50**:984 (Nov. 15) 1924.
4. Schultz, P. J.: Ztschr. f. orth. Chir. **43**:528, 1924.
5. Ducroquet, R.: Rev. de chir. **62**:493, 1924.

cation, and the roentgenogram showed a well formed head in the acetabulum. The second patient was aged 20 months, and the dislocation was bilateral. The femoral heads could be palpated and the roentgen-ray examination confirmed the diagnosis of double congenital dislocation. Reduction was attempted and a plaster spica was applied. Three months later, new roentgenograms showed that the luxation had recurred. It was decided again to make an attempt at reduction, but before this was done roentgenograms were made, and these showed the hips to be reduced. The case has been followed, and the hips have remained in place. Ducroquet concludes that spontaneous reductions only occur in the anterior type of dislocation. He believes that the head of the femur descends, little by little; the epiphyseal nucleus increases in size, and finally the roof of the acetabulum becomes more and more horizontal over the head. Two theories have been advanced to explain spontaneous reduction, but neither is completely satisfactory. The first supposes that trauma and exercise caused by the performance of certain movements produces a sort of voluntary reduction, and that this repeated many times a day finally causes the hip to be replaced. The other theory is based on the belief that congenital dislocation is due to anteversion of the femoral neck. Anteversion of the neck is normal in the fetus, but is corrected with growth. Congenital dislocation is due to arrest of development, and spontaneous reduction may be brought about by the resumption of normal development and correction of the anteversion of the neck. It seems true, from Ducroquet's report, that a mild type of luxation may reduce spontaneously before the eighteenth to twenty-fourth month.

Absence of Sacrum.—Stewart [6] reports an absence of the sacrum in a Mexican boy of 6 years, who had no control over the bladder and bowels. There also existed double clubfoot and some deformity of the low spine at the time of birth. The boy sat upright at 18 months and walked at 2 years. He became very active on his feet and was said to be of normal mentality. Roentgen-ray examination showed a complete absence of the sacrum and coccyx. The ilia were articulated with the transverse processes of the fifth lumbar vertebra and apparently also with the spinous process. The pelvic inlet was decreased in transverse diameter and was oval in shape.

SCOLIOSIS

Treatment of Scoliosis by Different Method from That Usually Employed.—Lovett and Brewster [7] have applied a plaster jacket, which

6. Stewart, S. F.: Absence of Sacrum, Arch. Surg. **9**:647 (Part 1) (Nov.) 1924.

7. Lovett, R. W., and Brewster, A. H.: J. Bone & Joint Surg. **6**:847 (Oct.) 1924.

is used as a mold, to the trunk in scoliosis. On this mold another jacket is made, from which, at the apex of the curve in the spine, a segment is removed. On the opposite side of the jacket, a hinge is applied, opposite the curve, and the segment is then pried open by a turn-buckle appliance applied opposite the concavity of the curve. In this way the trunk is stretched out. The advantages of this method are that the pressure is widely distributed, and that the hinge on the side of the jacket acts as an eccentric on which the trunk is extended. The screw in the turn-buckle gives irresistible force and, as it were, the ends of the arch are pulled out so that the arch may collapse. During this process, the authors have noticed that rotation disappears with the lateral correction. The authors present roentgenograms demonstrating improvement and correction of scoliosis.

[ED. NOTE.—We feel that this method suggested by Brewster points the way to a marked improvement in the treatment of scoliosis.]

Subsequent Report of Treatment of Structural Scoliosis at the Massachusetts General Hospital.—Klein [8] reports on the treatment of scoliosis by exercises and corrective jackets which, acting together, supplement one another. The pelvis and thorax are rotated in opposite directions, with the aim of unwinding the spine and extending it. The peripheral force applied by the plaster cast and further padding, together with the pressure of the forced respiratory exercises, changes the conformity of the thorax. Windows in the cast allow further correction of the trunk with the forced breathing.

[ED. NOTE.—We feel that marked improvement has been obtained by Klein in old cases of fixed scoliosis. This improvement is shown by increased expansion of the chest, by better general nutrition and health, and by improved symmetry of the body.]

RICKETS

Signs of Early Rickets.—Moore [9] has studied mild cases of rickets, and has found a means of recognizing the presence of the disease at its first beginning. He believes that the head and thorax are first to be affected and has found that craniotabes was present in 60 per cent. of his cases. The square, triangular and oval forms of the chest at the fifth costochondral junction were noticeable. Knock-knee and bow-leg are always preceded by abnormal lateral mobility in the knee joint, which is often the first sign of rickets in the lower extremities.

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8. Klein, Armin: J. Bone & Joint Surg. **6**:853 (Oct.) 1924.

9. Moore, C. U.: Newer Clinical Signs of Early Rickets, J. A. M. A. **83**: 1469 (Nov. 8) 1924.

Underlying Cause in Pathogenesis of Rickets—Findlay [10] recognizes that five important factors affect favorably the metabolism of the individual in rickets. These five factors are sunlight, exercises, vitamin, calcium and phosphorus. He says, however, that the true exciting cause of rickets has not yet been disclosed. Sunlight and cod liver oil will not always cure rickets, and no individual factor seems to be a specific. He believes that the most characteristic feature of rickets is the deficient calcium content in the blood, and that it is not merely a disease of the bones. From recent metabolic studies, he concludes that there is a diminished absorption of the calcium available in ample amount in the diet. Findlay suggests that rickets is primarily a disease of intestinal origin and probably of an infectious nature.

TUBERCULOSIS

Tuberculosis of the Knee.—Allison [11] emphasizes the importance of making a definite diagnosis in tuberculosis of the knee. He believes that in suspected cases, that is, those in which the circumstantial evidence points definitely to tuberculosis as the disease process, operation should be performed for the purpose of establishing a positive diagnosis. Tissue should be examined and animal inoculation done. This course is justifiable because the disease process, where it exists, will more or less completely destroy the knee, and will act as a menace to the life and limb of the person diseased. A Wassermann test should be a routine procedure in a study of the etiology of knee joint disease. In case the tissue examination by the microscope shows no evidence of tuberculosis, or in case the guinea-pig inoculation shows, after a proper period of time, no evidence of tuberculosis, then it may be safely assumed that the knee joint in question is free of tuberculosis. It is perhaps more frequent than is generally realized for a person to have syphilis as well as knee joint tuberculosis. It is essential for those who attempt to estimate the value of therapeutic measures, such as heliotherapy, to establish a positive diagnosis of bone or joint tuberculosis in all cases included in their statistics.

Recent Contributions to the Subject of Heliotherapy.—Rollier stands alone as an exponent of the value of heliotherapy from the fact of his long experience and his unusual clinic. His dictum on this subject will be generally accepted as the result of long and careful study. He asks us to remember that the external manifestations of tuberculosis are no more than the local symptoms of a constitutional disease, and that in the rational treatment of surgical tuberculosis, reliance should be placed

10. Findlay, Leonard: Underlying Cause in Pathogenesis of Rickets, J. A. M. A. **83**:1473 (Nov. 8) 1924.

11. Allison, Nathaniel: Tuberculosis of Knee; Importance of Diagnosis, J. A. M. A. **83**:750 (Sept. 6) 1924.

chiefly on the therapeutic resources of nature. He emphasizes more than formerly that the sun acts through its whole spectrum and not by virtue of one group of rays. Weisner has found that the infra-red rays have bactericidal power and exert a direct influence on deep seated foci. Block shows their vasodilator action, and recent experiments led him to conclude that under the influence of direct sunlight the blood becomes a receptacle for radiant energy.

LoGrasso,[12] from his experience at the John W. Adams Hospital, believes, with Rollier, that motion within the limit of pain in tuberculous joints is beneficial and prevents atrophy and ankylosis, and that plaster casts are not compatible with heliotherapy. He also believes strongly in the efficacy of the direct sunlight in comparison with artificial rays. Deep pigmentation increases the effectiveness of the sun's rays, possibly by transforming the light waves so that they penetrate more deeply.

Remote Results of Treatment in Pott's Disease.—Jentzer [13] reports the end-results in thirty cases of Pott's disease in which operations were done to fuse the spine. In four of these cases, celluloid splints were introduced after the method of Lange. In the others, bone transplants were used according to the Albee technic. The disease process varied in its severity, and the age of the patients also varied. As a rule, there was a prolonged period of recumbency preceding operation. In addition to recumbency, heliotherapy was employed, and injections and frictions of Gamelan were used. The author believes that the latter has been demonstrated to be of value. Operation was done when it was determined that the patient had been built up to the point where the blood examination showed a relative lymphocytosis. The preoperative treatment usually improved cases in which there was paraplegia. In four cases in which no improvement was obtained after a long period, operation proved to be of striking benefit. One case unimproved after eighteen months of recumbency cleared up within a few weeks following the fusion operation. Jentzer believes that prolonged after-treatment is extremely important and concludes from his study that the total period of treatment may be greatly decreased by operation and that the results with operation are better than without it.

Tuberculous Spondylitis.—Leskinen [14] has made a statistical report on the analysis of 220 conservatively treated cases of tuberculosis of the spinal column. Of these cases, 52.3 per cent. were in males. Eighty-one and four tenths per cent. of the patients were from 1 to 15 years of of age. The cervical region was affected in 16.2 per cent., the thoracic

12. Recent Contributions to the Subject of Heliotherapy, J. Bone & Joint Surg., October, 1924, p. 920.

13. Jentzer, A.: Rev. méd. de la Suisse Rom. **44**:577 (Sept.) 1924.

14. Leskinen, S: Acta chir. Scandinav. **57**:193 (Aug. 13) 1924.

region in 56.4 per cent., and the lumbar region in 27.4 per cent. of the cases. Abscesses occurred in the following ratio: Cervical, thoracic and lumbar, 1:3, 3:5 and 1:8. Detailed information was obtained in 137 cases. There was a mortality of 40.5 per cent. Twenty-six and three tenths per cent. of this mortality occurred in cervical tuberculosis, 46.3 per cent. in thoracic, and 34.1 per cent. in the lumbar cases. In the male cases alone, there was a 50 per cent. mortality, while in the female the mortality was 32.1 per cent. Death occurred within the first two years in 74.9 per cent. of all cases. The death rate was higher among patients under 20 years of age, and lowest among those patients between 20 and 30. Complete recovery was obtained in 30.4 per cent. of the cases. As to the regions affected, the cervical cases recovered in 69.5 per cent., the thoracic in 21.1 per cent., and the lumbar cases in 34.1 per cent. Mortality was higher among patients giving a history of tuberculosis in their families. Complete recovery was reported as being 28.9 per cent. in those who had hereditary tuberculosis, and 31.1 per cent. in those who had no such family history. In all cases in which complications arose involving the nervous system, the outcome was fatal. Complications which arose due to abscesses increased the mortality rate 49 per cent. and reduced the complete recovery rate to 17.6 per cent. In those cases in which tuberculosis was found to exist in other organs, the result was almost always bad.

[ED. NOTE.—These surprising figures on the mortality rate in Pott's disease suggest the necessity for an estimation of the results of this disease in other countries.]

Demonstration of Specimen of an Albee Graft of Spine.—Pusch [15] has examined a specimen of a spine in which there was Pott's disease involving the tenth, eleventh and twelfth dorsal vertebrae. The patient, a child of 14, had been treated by the insertion of an Albee graft uniting six spinous processes nine years earlier. The history is given of a remission of several years, with subsequent increase of the kyphos and death due to amyloid degeneration. The author states that although the graft prevented an increase in deformity of the primarily affected vertebrae, it did not check the further progress of the disease, which resulted in the formation of a kyphos above the graft.

Aim and Fate of the Albee Graft.—Biesalski [16] bases his report on 100 Albee operations and on the examination of eight specimens. In the latter he found that the graft had not grown with the spine, either in length or in width. Owing to the danger of pseudarthrosis, the author questions the advisability of subjecting an operated spine to early functional strain. He believes that the protection given by the graft is not

15. Pusch: Ztschr. f. orthop. Chir. **45**:369, 1924.
16. Biesalski, K.: Arch. f. klin. Chir. **127**:667, 1923.

sufficient to prevent the progress of the disease but that when the destructive process is no longer active, the grafted bone may act as a corset in the after-treatment.

[ED. NOTE.—Fusion operations may be of value in children, but Albee's operation is not advisable on growing spines. No type of operation should be performed during active disease.]

OSTEOMYELITIS

Brodie's Abscess.—Henderson and Simon [17] report thirteen cases of Brodie's abscess which have been seen in the last ten years at the Mayo Clinic. They believe that the pathologic process in Brodie's abscess has certain characteristics. It is a focus of infection situated in cancellous bone near the epiphyseal line and arising as a remnant of a former osteomyelitis, or it may be a sharply localized focus of uncertain origin. There is often a period of latency, during which the resistance of the body and the sclerosing wall of bone about the abscess seem to hold the process in check. At any time, however, it may burst into activity as a result of lowered resistance, perhaps associated with trauma or other acute infection. Sinuses will then form and a sequestrum may be discharged. An extensive destruction of the diaphysis may follow. The condition is not of tuberculous origin. Treatment should be surgical and should be applied to the location of the abscess, and will result in cure in the majority of cases.

[ED. NOTE.—In our experience, several typical Brodie's abscesses have been proved to be of tuberculous origin.]

ARTHRITIS

Focal Infection and Arthritis.—Stauffer [18] has studied at the Presbyterian Hospital in Philadelphia 300 patients with regard to focal infections and consequent arthritis. In a group of 200 patients who had arthritis, 66⅔ per cent. had diseased tonsils. Twenty-five per cent. had infection of their sinuses. He concludes that the enthusiasm to extract all teeth in advanced cases of arthritis should be discouraged. The indiscriminate removal of tonsils is also unnecessary. In the earlier stages of arthritis, removal of these infected foci may put the patient on the road to recovery. After the arthritis has become established, there is grave question as to the advisability of tonsil and teeth removal. The author believes that the effect of the shock of any operation on helplessly crippled arthritic patients should be seriously considered.

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17. Henderson, M. S., and Simon, H. E.: Arch. Surg. **9**:504 (Part 1) (Nov.) 1924.

18. Stauffer, N. P.: M. J. & Rec. **120**:542 (Dec. 8) 1924.

Synovectomy in Chronic Infectious Arthritis.—Swett,[19] who has reported in previous papers the results of synovectomy in chronic arthritis, adds twelve more cases to his series. He finds the operation to be warranted in certain cases of chronic infectious arthritis. He believes it will promote the restoration of function to the joint and that it may be expected to prevent further destruction of the cartilage and consequent ankylosis. The operation should be done to remove the synovial membrane before great damage to the bone and cartilages has been done. Synovectomy is indicated in certain cases, but the benefit derived from the operation seems to be in direct proportion to the extent of the pathologic changes that have taken place in the joint.

Lactic Acid in Arthritis and Rheumatoid Conditions.—Cajori, Crouter, and Pemberton [20] have carried out a series of experiments to ascertain whether or not there is a deviation from normal physiology in arthritis, as is implied in the lactic acid theory, and have reached the following conclusions: 1. The lactic acid contents of the blood, urine and sweat of patients suffering from arthritis and rheumatic disabilities has been determined and the results have been compared with the respective lactic acid contents from nonarthritic persons. The lactic acid was determined also in the synovial fluid from a case of joint effusion. In no case have they observed abnormal quantities of lactic acid in arthritic patients. These findings, therefore, lend no support to the idea that arthritis, at least of the types studied, is caused or characterized by abnormal production or disposal of lactic acid. 2. Lactic acid has been found to be present in sweat in considerable quantities, making up about 50 per cent. of the organic acids of the sweat. Its presence in this secretion may be referable to the chemical changes occurring in the sweat glands during their activity. 3. The benefit accruing to arthritic patients from sweating measures cannot, in the light of these results, be ascribed to the elimination of lactic acid in the sweat.

Scarlatinal Arthritis.—Joe [21] has gone over the records of 25,000 cases of scarlet fever and found that arthritis recurred in 3.75 per cent., and that it was much less frequent in children. Joint symptoms appeared usually on the seventh day, and in 63 per cent. of the cases arthritis was the sole complication.

Tardy Arthritis from Typhoid Bacilli.—Dufour and Baruk [22] report a case of purulent arthritis of the knee which developed as a sequel to

19. Swett, P. P.: J. Bone & Joint Surg. **6**:800 (Oct.) 1924.

20. Cajori, F. A.; Crouter, C. Y., and Pemberton, R.: Lactic Acid in Arthritis and Rheumatoid Conditions, Arch. Int. Med. **34**:566 (Oct.) 1924.

21. Joe, A.: Edinburgh M. J. **83**:341 (June) 1924.

22. Dufour, A., and Baruk, A.: Bull. et mém. Soc. méd. d. hôp. de Paris **48**: 1383 (Oct. 23) 1924.

an acute generalized arthritis, from which the bacillus of typhoid was isolated. The patient promptly recovered after treatment with vaccines. The patient had had typhoid fever eight years before, and the authors assume that the infection in the joints had remained latent for this period.

Pneumococcus Arthritis After Pneumonia.—Taccone [23] believes that the onset of pneumococcus arthritis after pneumonia is usually abrupt. He divides the types presented into three varieties: rheumatoid or arthralgic, serous and suppurative. The usual characteristics of the joint involvement are a marked periarticular swelling, and edema, which may extend throughout the entire limb, and an absence of any reddening of the skin. Spontaneous cure is possible, but cure usually follows the evacuation of pus. In the joint fluid, it is usually possible to demonstrate the pneumococcus. Sometimes the infection is mixed, pneumococcus and streptococcus, staphylococcus, etc. The prognosis, in general, is favorable. It is more favorable in infancy than in adult life. It is less favorable when polyarticular. The results as regards restoration of anatomic and functional integrity of the joints are uncertain, but may be satisfactory. In the hip joint, various serious complications may occur, as dislocation of the head, developing as late as nearly two years after the acute illness, or the epiphysis may be displaced or destroyed. The treatment of choice was formerly arthrotomy or puncture. Now the author believes a single or numerous aspirations, combined with the use of vaccines, preferable. The autogenous method is the more desirable method in a majority of the cases. Diathermy is, he believes, very much contraindicated, especially in the acute stages. He reports one case involving a shoulder joint in which several aspirations combined with autogenous vaccines gave an excellent result.

Syphilitic Arthritis with Eosinophilia.—McChesney, Kemp and Resnik [24] report two cases of syphilis showing acute polyarthritis with eosinophilia. In one case with acute hydrops of the knee, *Spirochaeta pallida* was recovered from the synovial fluid.

PARALYSIS: POLIOMYELITIS, SPASTIC AND OBSTETRIC

Poliomyelitis, with Especial Reference to Treatment with Rosenow's Serum.—During the poliomyelitis epidemic of 1916 in Yellowstone County, Montana, Clarke [25] observed twenty-four cases, eighteen of which were treated with Rosenow's serum. In this series of cases there was one death. The number of patients recovering with paralysis was

23. Taccone, G.: Pediatria **32**:1228 (Oct. 15) 1924.

24. McChesney, A. M.; Kemp, J. E., and Resnik, W. H.: Bull. Johns Hopkins Hosp. **35**:235 (Aug.) 1924.

25. Clarke, F. B.: California and West. Med. **22**:437 (Sept.) 1924.

eight, or 47 per cent., and the number of patients recovering without paralysis was nine, or 52 per cent. Of the eight patients paralyzed, in five the paralysis was moderately severe, in three it was very mild. When one considers that in various epidemics, the general mortality rate is 25 per cent., but that in this series only one death occurred, he must conclude either that the administration of Rosenow's serum was of value or that the disease was unusually mild. However, during the same year in the same state, the official statistics reported a death rate of 40 per cent. in those cases of paralysis in which Rosenow's serum was not used.

Epidemiology of Poliomyelitis.—Gioseffi [26] reports on the epidemiology of poliomyelitis, as shown in the cases occurring in Istria in 1914. In almost all instances there was close, direct or indirect, association of the cases. (It is of interest to note that in this region where the disease was almost unknown previous to 1909, the disease was frequently fatal and there were often two or more cases in one family. It appeared to be directly contagious in school and church groups.)

[Ed. Note.—This would seem to argue for a considerable degree of acquired immunity in countries where the disease has been prevalent.]

Roentgen-Ray Treatment of Poliomyelitis.—Turano [27] reports that thirty cases of infantile paralysis have been treated at the Institute for Roentgenology and Electrotherapeutics at Rome. Of these, thirteen cases have been treated long enough to allow of certain deductions. Twelve cases showed marked improvement in a comparatively short time. In one the improvement was slight. His conclusions are: 1. Roentgen rays act beneficially in anterior poliomyelitis. No other method of treatment commonly used in this disease can show results equal to those obtained by this method. 2. Irradiation of the affected cord segment should be done within a few days of the onset of the disease, before irreparable damage is done to the nerve cells. 3. The action of the rays consists in a definite antiphlogistic action and secondarily in a slight stimulating effect on the cells not affected by the disease process.

[Ed. Note.—The cases were evidently carefully studied before and during the treatments, and the results seem suggestive.]

Arthrodesis of Shoulder for Deltoid Paralysis.—Asplund [28] reports end-results of arthrodesis of the shoulder in eight cases of infantile paralysis. The reexamination, in all cases, was performed ten years after the operation. In seven cases out of the eight, the functional

26. Gioseffi, M.: Riforma med. **40**:826 (Sept. 1) 1924.
27. Turano, Luigi: Pediatria **32**:1081 (Sept. 15) 1924.
28. Asplund, G.: Acta chir. Scandinav. **57**:310 (Aug. 13) 1924.

result is described as satisfactory, in two cases as very satisfactory, while all the patients are reported to have derived decided practical benefit from the operation. The following points are emphasized: 1. Age is of no consequence. The best result was obtained in a boy operated on at the age of 4 for bony ankylosis. 2. Bony ankylosis was obtained in four cases, fibrous in three. The latter also are satisfactory functional results. 3. There is no evidence of a greater degree of shortening in the younger patients as compared with the older ones. The shortening varies from 3 to 5 cm., and is chiefly to be explained as due to the general atrophy of a paralytic extremity. The author found the same amount of shortening in unoperated cases. 4. Active abduction varied, in cases studied, from 50 to 150 degrees. 5. No scoliosis of any importance has resulted from the operation in any case. 6. The author warns against fixation in too great abduction; from 80 to 90 degrees is sufficient. 7. Slight external rotation is very necessary in order to counteract the tendency to pronation. 8. The operative procedure is arthrodesis "as described by Vulpius." Joint surfaces are denuded of cartilage without any bone graft and without any plastic operation on the acromion.

Indications for Sympathetic Ramisection, Together with Observations on Muscle Tone.—Royle's [29] own words are:

> The main indication for sympathetic ramisection is the presence of excessive plastic tone. The greatest benefit comes to those patients whose movements are obstructed by the tendency to maintain positions attained by active contraction. The second necessity is adequate cortical control. No beneficial result can be expected if the cortical areas concerned with the representation of movement or of the position of the limbs are destroyed. Similarly, any process which effectively blocks cortical control must constitute a contraindication, since gain is a physical impossibility, and the uninhibited activity of subcortical centers would so dominate the clinical picture that the mere removal of plastic tone would have little beneficial effect. Imbecility and some degrees of mental deficiency would render operative treatment a waste of time and energy. To justify surgical interference, the lesion must not be progressive. This particularly applies to spinal conditions, and more especially when the spinal lesion is accompanied by muscular wasting.

Treatment of Cerebral Spastic Paralysis, with Special Reference to the Stoffel Operation.—Dickson [30] is convinced of the value of the Stoffel operation in reducing spasticity, relieving contractures, and improving local conditions. He believes, also, that there is an improvement in the general condition when the spasticity is relieved in the extremities, this being due to the quieting effect of the operation on the complex reflexes through which the coordination of the activities of

29. Royle, N. D.: M. J. Australia **1**:333 (Sept. 27) 1924.

30. Dickson, F. D.: Treatment of Cerebral Spastic Paralysis, with Special Reference to the Stoffel Operation, J. A. M. A. **83**:1236 (Oct. 18) 1924.

the body is carried out. He reports thirty-nine cases, in which the results were excellent in 25 per cent., 33 per cent. good, and 35 per cent. fair.

Birth Paralysis.—Valentin [31] describes the pathologic changes in a case of grave double birth palsy in a child of 9 months, who died during an operation for relief of brachial palsy. He found a great change in the cervical section of the spinal cord, especially in the anterior horn area. He points out the importance of examining the spinal marrow in each case of birth palsy which comes to necropsy, and believes that the damage to the cord is done at the time of birth, but he is willing to admit that intra-uterine damage cannot be ruled out.

Volkmann's Ischemic Paralysis.—Deniker [32] reports a case of Volkmann's paralysis seen in a young girl, with contractures of the third and fourth fingers. The paralysis in this case did not follow fracture. The patient suffered a compression of the arm without fracture, which was followed by large hematoma. Denucé, in 1920, observed the rôle played by the sympathetic nerves in so-called ischemic paralysis, and Deniker's case would seem to follow along the lines of explanation suggested by Denucé.

NEOPLASMS

Hemangioma of the Sciatic Nerve.—Stewart and Bettin [33] report an interesting tumor of the sciatic nerve in a boy of 10. A lump had been present since the age of 1 year. Gradually this had enlarged, and recently there had been severe neuritic pain and muscle weakness. An exploratory operation was performed, and the internal popliteal nerve was found to be from five to six times its normal diameter and presenting a mottled brownish appearance. Later, the leg was amputated and the specimen obtained. The tumor was a plexiform telangiectasis, with a tremendous outgrowth of thin-walled blood vessels which invaded the surrounding nerve and muscle tissues. In this sense it was malignant, although there were no metastases.

Giant Cell Tumors.—Herendeen [34] advocates the treatment of giant cell tumors by radiation. He believes that the roentgen-ray appearance is sufficiently characteristic to establish the diagnosis, and that treatment by radiation may be relied on to produce growth restraint and firm encapsulation of the tumor and to give relief of pain. He claims that the treatment brings about a more rapid ossification than does surgical intervention and that in many cases it obviates the loss of the limb by amputation. The treatment is followed by a reaction which is obvious,

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31. Valentin: Ztschr. f. orthop. Chir. **45**:337, 1924.
32. Deniker: Bull. et mém. Soc. nat. de chir. **50**:76 (Feb. 2) 1924.
33. Stewart, S. F., and Bettin, M. E.: Surg., Gynec. & Obst. **39**:307 (Sept.) 1924.
34. Herendeen, R. E.: Am. J. Roentgenol. **12**:117 (Aug.) 1924.

clinically and roentgenologically, and which simulates rapid growth of the tumor. Pain and tenderness diminish as the reaction subsides, ossification takes place and function returns.

Lewis [35] reports seventeen cases of giant cell tumor of the vertebrae. Recovery after partial removal or no attempt at removal occurred in thirteen cases. The four deaths could not be attributed to malignancy of the tumor, nor were there metastases in any case, although there was local recurrence in four. Good results were obtained from the use of irradiation as well as from partial excision. Lewis stresses the rôle of trauma in the production of these lesions and asserts that many of them represent reactive growths to this stimulus. Such a reactive growth may histologically resemble a giant cell sarcoma when, biologically, it should be regarded as a chronic reparative process. This group of cases raises doubts as to the nature of many of the giant cell tumors and their biologic significance.

Burlend and Harries [36] describe a white myeloma of the radius which occurred in a girl of 9 following a Colles' fracture. Removal of the tumor and insertion of a bone graft were followed by a good functional result. They find evidence that the giant cells of a benign epulis or giant cell myeloma are derived from osteoclasts. They believe that the removal of the marrow by giant cell phagocytosis and the formation of tumor cells by fragmentation of the giant cells are similar to the differential changes that occur in certain cells in tissue culture. They note the presence of certain giant cells in the myeloma with nuclei exhibiting an uncommon type of karyokinesis similar to that seen in certain protozoa.

Echinococcus Cyst of Bone.—Joannides and Riley [37] report a case of hydatid cyst in a woman, 45 years of age, of Greek origin. The cyst was loosely attached to the scapula and chest wall. It was removed by operation, and there was no recurrence after six months. Costantini [38] has made a study of hydatid cysts of the long bones and reports a very high percentage of cures following careful and wide removal of the entire area of disease. The cysts may be unilocular or multilocular, and a point to be studied is whether they are produced by the same or by different parasites.

Primary Multiple Endothelioma of Bone.—Kolodny [39] reports a case of primary multiple endothelioma of bone, and calls attention to

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35. Lewis, D.: Primary Giant Cell Tumors of Vertebrae, J. A. M. A. **83**: 1224 (Oct. 18) 1924.

36. Burlend, T. H., and Harries, D. J.: Brit. J. Surg. **12**:254 (Oct.) 1924.

37. Joannides, M., and Riley, W. A.: Echinococcus Cyst in Scapular Area, Arch. Surg. **9**:537 (Part 1) (Nov.) 1924.

38. Costantini, H.: Rev. de chir. **62**:401, 1924.

39. Kolodny, A.: Primary Multiple Endothelioma of Bone, with Special Emphasis on Its Roentgenologic Features, Arch. Surg. **9**:636 (Part 1) (Nov.) 1924.

the roentgenologic features. Ewing states that there is a diffuse absorption of bone, without a trace of bone production. The writer, however, cites his case and one of Ewing and one of Phemister, and says that careful study of the roentgenograms shows that there is definite bone production. He does not claim that all endotheliomas will show bone production, but that the reverse is not true.

Sarcoma of Bone.—MacGuire and McWhorter [40] report a study of fifty cases of bone sarcoma in which the diagnosis was checked by microscopic examination of tissue. In respect to diagnosis, they conclude that with clinical, roentgenologic and pathologic study, one should be able to arrive at a diagnosis of sarcoma in every case, and in about 90 per cent. be able to distinguish between osteogenetic, giant cell, round cell and endothelial tumors. Further differentiation is purely arbitrary.

Hitzrot [41] likewise believes that it is only possible to arrive at a correct diagnosis in a case of bone tumor after proper consideration of all the evidence gained from the history, clinical and roentgen-ray examination, and by consultation with the roentgenologist and pathologist. In many cases this must be supplemented by a pathologic diagnosis from the tumor itself. Ewing believes that the therapeutic test by radiation should first be employed. Coley, Bloodgood, Codman and others believe that a proper investigation of the tumor with tissue study by a group of competent pathologists is a safer procedure. Hitzrot agrees with this view, but urges that en bloc removal of the tumor bearing bone should be the procedure of choice in suitable cases, both for diagnosis and as a therapeutic measure.

UNCLASSIFIED DISEASES OF BONE: TRAUMATIC, TOXIC AND GROWTH DISTURBANCES

Osteochondritis Deformans, Juvenilis, Legg's Disease.—Tillier,[42] discussing osteochondritis deformans juvenilis of the hip, states that neither from the clinical nor roentgenologic point of view is there any evidence for an infectious origin of the process. He considers that the cause of the condition is developmental in nature. He notes many points in common between congenital subluxation of the hip and osteochondritis, and calls attention to the fact that the two are often associated. There also is a similar evolution in both conditions, which favors the belief in a common cause. He believes that both are dependent on a congenital etiologic factor, one producing a subluxation and the other an osteochondritis.

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40. MacGuire, C. J., Jr., and McWhorter, J. E.: Sarcoma of Bone, Arch. Surg. **9**:545 (Part 1) (Nov.) 1924.
41. Hitzrot, J. M.: N. Y. State J. Med. **24**:790 (Aug.) 1924.
42. Tillier, R.: Lyon chir. **21**:464 (Aug.) 1924.

Koehler's Disease of the Metatarsal Head.—Payr,[43] discussing a demonstration by Sonntag, his assistant, of six cases of Koehler's disease of the second metatarsal head, states his own view that the necrosis of the head is caused by a mechanical disturbance of the circulation of that part of the bone. Up to this point he agrees with Axhausen, but he does not accept the latter's rather artificial hypothesis of an embolic infarct. Payr believes that the more probable explanation is that the circulation is interrupted by damage to the capsular vessels, which are responsible for the nutrition of the epiphysis. The predisposition to injury here is readily explained by the anatomic arrangement and by irrational shoes. High heels produce a contracted position of the toes, with hyperextension of the proximal joints, leading to a compression of the vessels. Very narrow shoes may press the lateral sesamoid bone against the capsule of the second metatarsal head.

CIRCULATORY DISTURBANCES

Periarterial Sympathectomy.—The operation of periarterial sympathectomy continues to be the subject of much attention in the current literature. Some of the reports are favorable and others unfavorable. Jiano,[44] from Bucharest, reports excellent results in a series of thirty cases which include a wide variety of conditions, such as syphilis, tuberculosis and central nervous system disorders. He explains the benefit obtained in dry gangrene as due to the relief of spasm in the smaller vessels and arterioles. In such cases the spasm is due to local irritation and is superimposed on a preexisting mechanical block. He considers sympathectomy a valuable procedure in torpid syphilitic lesions, the improvement here being due to the vasodilatation in the distal part of the limb which always follows the operation and to the freer access of blood. He believes that in such cases the blood supply is often inadequate and that this prevents the specific drugs from reaching the part. There were only two failures, one a tuberculous knee and the other a pelvic neuralgia. He describes two technical points that he considers important. After stripping the outer coat, he wraps the artery with a pedunculated flap of fascia and in addition places a loose ligature about the artery above the site of operation, the ends being brought out of the wound so they may be tied in case of emergency.

Petrescu[45] reports a series of fifteen cases with favorable results. Healing of an old extensive leg ulcer began in three days following an extensive sympathectomy and resection of the saphenous vein. Recovery was complete in from one to three weeks in all the cases of trophic

43. Payr, E.: München. med. Wchnschr., Nov. 21, 1924, p. 1668.
44. Jiano, J.: Rev. de chir. **62**:482, 1924.
45. Petrescu, G.: Lyon chir. **21**:449 (July-Aug.) 1924.

ulcer, mal perforant, etc. In gangrene, the pain was relieved at once and amputation could be performed under better conditions.

Black,[46] from Singapore, reports ten cases of leprosy, with ulcers of the feet, in which periarterial sympathectomy was done. Healing followed the operation in all but one case. He feels that the results are encouraging, but that sufficient time has not yet elapsed to allow him to draw definite conclusions from these cases.

Hybner[47] also has had favorable experience with the operation. He has compiled from the literature reports of 100 cases, and has analyzed the results. He concludes that durable results have not been obtained in angiospasm or in gangrene. In other conditions the results have been good. He feels that the operation represents a broadening of surgical therapy and that the ease with which it may be done ought to recommend it when other means have failed.

That there may be danger from enthusiasm, leading to the application of the operation in conditions in which benefit cannot reasonably be expected, is indicated in some of the articles abstracted above. To evaluate the operation accurately, we must depend on reports that show that the judicial attitude has been maintained.

The study by Allen[48] is important in this sense. He reports eight cases of thrombo-angiitis obliterans of Buerger treated by this method. He concludes that periarterial sympathectomy can be performed without ill effects to the patient, that characteristic reactions usually follow the procedure, that improvement does not always follow when characteristic reactions are obtained, and that slight benefit may occur when they are completely absent. In thrombo-angiitis obliterans, he does not consider the beneficial results sufficiently lasting to justify the operation. In carefully selected cases of arteriosclerotic gangrene, the results are sufficiently good to warrant its further trial.

That the operation is not without danger is shown by a report by Rieder[49] of complications encountered in three cases. One patient died from extensive thrombosis of the femoral artery two days after operation. The second developed severe disturbance of the circulation which necessitated amputation. In the third, the femoral artery was torn during the operation. Rieder believes that beneficial effects may result from the dissection of the many little nerves accompanying the artery and that they are not necessarily due to the removal of the adventitia with the sympathetic tissue. In support of this view, he reports three cases in which from an operation in the neighborhood, but not touching

46. Black, K.: Brit. M. J. **2**:165 (Aug. 2) 1924.
47. Hybner, L.: Lyon chir. **21**:542 (Oct.) 1924.
48. Allen, A. W.: Boston M. & S. J. **191**:391 (Aug. 28) 1924.
49. Rieder, W.: Zentralbl. f. Chir. **51**:1685 (Aug. 2) 1924.

the artery itself, striking effects were seen in respect to the healing of severe ulcerations of the leg, effects similar to those following periarterial sympathectomy.

New Method of Examination in Diseases of Circulation of Extremities.—Brooks and Jostes [50] have devised a new method for the diagnosis of circulatory diseases of the extremities. It depends on a careful study, by means of a thermocouple galvanometer, of temperature changes in the limb, under alternating conditions of obstruction of the circulation and release. From the results obtained in thirty-seven examinations of eighteen persons, they believe that the method gives valuable information as to the presence or absence of arterial disease in the extremity. It was found that in persons with presumably normal arteries, the temperature of the distal tissues fell during the period of arterial obstruction and rose immediately after the removal of the obstruction. In all persons with arteries known to be obstructed by disease, the temperature fell during the period of arterial obstruction but did not rise immediately after the obstruction was released. Similar curves were always obtained in repeated examinations of the same persons. The curve seemed to be characteristic of the condition that was present. A continued fall of temperature in the distal tissues after the tourniquet was removed was considered a sign of obstruction of the larger arteries.

Diathermy in Intermittent Claudication.—Lian and Descoust [51] have been much encouraged by the results obtained from the use of diathermy in intermittent claudication. They state that it has no effect on the large arteries, but only on the smaller vessels and the capillaries, and that this effect is beneficial. It relieves spasm and improves the metabolism of the tissues. In the beginning the treatment must be given every day, later every third day. The course consists of twenty applications, each of from thirty to forty minutes. The course should be repeated about every three months. In two patients remarkable improvement was obtained; in one the relief was slight, and in two patients with complete obliteration of the artery there was failure.

FOOT CONDITIONS

Hallux Valgus.—Jones,[52] discussing the treatment of hallux valgus, emphasizes the close association of both hallux valgus and hallux rigidus with flattened arches. The preventive treatment of hallux valgus consists in developing a heel and toe walk with parallel feet and in wearing anatomically correct shoes. The mechanical treatment consists in deflect-

50. Brooks, B., and Jostes, F. A.: Clinical Study of Diseases of the Circulation of the Extremities, Arch. Surg. **9**:485 (Part 1) (Nov.) 1924.

51. Lian, C., and Descoust, P.: Presse méd. **32**:833 (Oct. 22) 1924.

52. Jones, R.: Brit. M. J. **2**:651 (Oct. 11) 1924.

ing the body weight from the inner to the outer side of the foot and in relieving the painful joint from friction and pressure. Operations for correction of deformity with no functional disability should not be undertaken lightly and never unless the patient is prepared to wear appropriate boots. The choice of operation should be decided by the special circumstances of the case. For some he advises a plastic procedure, for the more severe he adds a cuneiform osteotomy on the inner side of the metatarsal head, and for the severe cases with arthritis he suggests the removal of the entire head of the metatarsal. For hallux rigidus cases he prefers to remove the base of the first phalanx. Where there is wide separation of the metatarsal heads, a condition that renders the fitting of shoes difficult, he suggests osteotomy of the base of the first metatarsal as an additional procedure.

LOW BACK PAIN AND SCIATICA

Diagnosis and General Problems.—Smith-Petersen [53] emphasizes the need for careful analysis of every sign and symptom in the examination of low back cases, and urges that an effort be made in every case to arrive at a precise diagnosis, particularly with respect to the differentiation of lumbosacral and sacro-iliac strains. He describes the procedure to be followed in the routine examination and points out that in making a diagnosis there is no one sign or symptom pathognomonic of a lesion affecting either the lumbosacral or sacro-iliac region, and that reliance must be placed only on the whole picture. The previous history, the patient's symptoms, and the distribution of pain in reference to the nerve roots should be carefully tabulated. Routine examination should include inspection, palpation, study of the movements in the standing, sitting and lying positions, straight leg raising and compression of the iliac crests. He attaches especial importance to reference of pain along the second and third sacral nerves and to limitation of movement and production of pain on straight leg raising, as pointing to a lesion of the sacro-iliac joints. In excluding lesions of the lumbosacral region, he depends particularly on freedom from pain and absence of limitation on hyperflexion of the bent knees on the abdomen.

Key [54] divides cases of low back pain into lesions of the lumbar spine, of the lumbosacral junction and of the sacro-iliac joints. He has made a study of 100 consecutive cases, and finds that they fall into three groups. First are those with injuries or disease in which a definite pathologic lesion can be demonstrated. These are about from 5 to 10 per cent. of the total. Second are those with chronic arthritis, which make up about from 30 to 35 per cent. of the whole. Third are those

53. Smith-Petersen, M. N.: J. Bone & Joint Surg. **6**:819 (Oct.) 1924.
54. Key, J. A.: Am. J. M. Sc. **168**:526 (Oct.) 1924.

with strains of the lumbosacral region or of the sacro-iliac joints. Of these, he found from 80 to 85 per cent. to be of the former, and from 15 to 20 per cent. of the latter. Lumbosacral strains of sudden onset are the most common, comprising from 35 to 40 per cent. of the group. These, with the postural strains of the lumbosacral region, amount to 75 per cent. of the group. There also is an intermediate group of 25 per cent. which the writer terms lumbosacral strains of gradual onset. The writer believes that sacro-iliac strains are much less common than generally supposed, constituting only about one in five of the low back strains.

Forrester-Brown,[55] in describing the objective signs of sacro-iliac strain, says that tenderness over the posterior inferior iliac spine is the one infallible sign. In her experience it has always been associated with the characteristic history, and the cases which present it have been relieved by support of the sacro-iliac joint, whereas sciatica and the other types of backache have not been so relieved. Another sure sign, though not always present in mild cases, is pain when the iliac crests are jarred together.

Brackett,[56] discussing low back strain with particular reference to industrial accidents, states that the effects of injury must be considered in relation to previous conditions, either congenital or pathologic, in order to arrive at a just estimate of the exact situation. Thus, the different results that follow apparently similar types of injury may be understood if viewed with reference to a previously existing ostearthritis or a mechanically weak back. Congenital anomalies and structural changes, such as a misplaced sacrum, asymmetrical articulation and marked lordosis, are important etiologic factors in producing the result.

Osgood and Morrison,[57] writing on the problem of the industrial lame back, urge the importance of more careful examination and study of the patient. They emphasize the need for more anatomic knowledge, and conclude that the most valuable contribution that could be made to the subject would be a careful analysis of common lesions and their usual symptoms based not only on anatomic dissection, but also on clinical study of supposed pathology as well. They feel that a preemployment physical examination by a physician who knows not only his medicine but also his mechanics would greatly lessen the numbers of back cases in industry. Up to the present, this has been opposed by labor organizations.

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55. Forrester-Brown, M. F.: Edinburgh M. J. **31**:392 (July) 1924.

56. Brackett, E. G.: Low Back Strain, with Particular Reference to Industrial Accidents, J. A. M. A. **83**:1068 (Oct. 4) 1924.

57. Osgood, R. B., and Morrison, L. B.: Boston M. & S. J. **191**:381 (Aug. 28) 1924.

[Ed. Note.—All the foregoing articles urge the need for more careful study of the objective findings in back cases, and we are all aware of the tendency of the majority of physicians to content themselves with a cursory examination and a general diagnosis of low back strain. In this connection, we commend the article by Smith-Petersen as one that should be read and studied. The student and the general surgeon will find it profitable to follow his routine.]

Causes of Back Strain.—Bauman [58] believes that many cases of pain in the low back and leg are due to some lesion or abnormality of the lumbar transverse processes. Irritation from the pressure on the nerve trunks is, in his opinion, the explanation of the commonly associated neuritis. He reports a series of thirty-five cases treated by excision of the transverse process, with good results.

[Ed. Note.—We find ourselves opposed to such an application of a serious surgical procedure without a more careful analysis of the cases than is indicated by the article. From our own experience and that of others who have performed this operation, we feel convinced that this procedure has little indication in cases of low back pain.]

Whitman [59] believes that exaggerated lordosis due to forward tilting of the pelvis, with sharp angulation of the lumbosacral junction, is a cause of a special type of backache that has been overlooked. The abnormal relations of the pelvis can only be accurately estimated in lateral roentgenograms. Treatment of the condition is either by the application of a brace or by a Hibbs fusion operation.

[Ed. Note.—We agree with Whitman that sharp angulation of the lumbosacral junction is often a cause of low backache, but we are surprised to find that anyone should regard this as a new observation.]

BONE AND JOINT SURGERY

Surgery of the Knee Joint.—Allison,[60] discussing the surgery of the knee joint, states that our present conception of its importance is based on an appreciation of several simple facts. First, that in many clinical conditions a high percentage of disabled knees may be returned to normal knee-joint function by appropriate surgical interference. Second, that in many disease processes, notably tuberculosis, operation on the knee offers the one sure method of cure. Here the operation should have for its object the establishment of ankylosis. Until such time as the treatment of tuberculosis by heliotherapy has been perfected and made practical, this would seem to be the surest method of cure. Third, that in the acute infectious processes of the knee, operations to clean the

58. Bauman, G. I.: J. Bone & Joint Surg. **6**:909 (Oct.) 1924.
59. Whitman, Armitage: J. Bone & Joint Surg. **6**:808 (Oct.) 1924.
60. Allison, Nathaniel: Surg., Gynec. & Obst. **39**:409 (Oct.) 1924.

joint cavity or to establish drainage offer the only hope of conservation of knee-joint function. Fourth, that excellent function may be expected with a stiff, strong, weight-bearing knee. On the other hand, if the knee is insecure, painful or partially functioning, use of the lower extremity is inhibited or lost. Fifth, that by surgical measures it is possible to restore the lost function to a knee joint and to aid nature in healing the diseased knee.

Cyst of the Semilunar Cartilage.—Jean [61] reports three cases of cyst of the external semilunar cartilage of the knee. The cysts were similar in character, of about the thickness of the cartilage, and contained a thick yellow fluid. It was necessary to remove the entire cartilage with the cyst, except for the posterior portion. He has compiled fifteen other cases from the literature, making eighteen in all. Thirteen were in men and five in women. Most of the patients were aged between 16 and 20. There was usually a history of injury to the knee, followed by the rapid development of swelling, which persisted instead of subsiding. The cysts were multilocular and extended toward the outer edge of the cartilage. Some authors consider them of congenital origin, others as due to infection or trauma, and others as of vascular origin or the result of chronic inflammation of the cartilage, which is pseudocystic.

Arthroplasty.—Campbell,[62] writing on the subject of mobilization of joints with bony ankylosis, states that in no case should a joint be operated on when tuberculosis was the causative agent in the production of the ankylosis. The chance of lighting up a latent tuberculous focus is too great to warrant surgical intervention in even the most favorable case. When there is a materially shortened leg due to a destructive osteitis in early life, mobilization of a joint is not considered of sufficient advantage to justify the means. In case there is extensive scar tissue binding the skin to the bone, a preliminary plastic procedure is required. He also believes that the operation is contraindicated in conditions of extreme muscle atrophy, such as found when bony ankylosis has existed for a long time or when there is dense, eburnated bone for a considerable distance on both sides of the joint. All evidence of acute infection must have subsided and osteoporosis must have disappeared before surgical measures can be instituted. He considers the indications for arthroplasty rare in those joints in which action may be compensated for by motion in adjacent articulations, as, for example, the shoulder and ankle. From personal experience he regards the percentage of success that may be obtained in well selected cases in the four favorable joints as follows: temporomaxillary, 90 per cent.; elbow, 90 per cent.;

61. Jean, G.: Bull. et mém. Soc. nat. de chir. **50**:775 (July 5) 1924.

62. Campbell, W. C.: Mobilization of Joints with Bony Ankylosis; Analysis of 110 Cases, J. A. M. A. **83**:976 (Sept. 27) 1924.

hip (single), 60 per cent., and knee, 75 per cent. He concludes as follows: 1. There is vast difference between arthroplasty and excision. The former is the reconstruction of a joint, the latter the induction of pseudarthrosis. 2. Our efforts should be directed toward reproducing function and not mere anatomic detail, thus simplifying and standardizing operative technic. 3. Fear of removal of too much bone is unwarranted, if one remains within the bounds of reason. Unstable joints are the results of atrophy and not of excision of bone. 4. The roentgenograms taken after several months show extensive reactive proliferation about the margins of the articular facets, but not a true arthritis. Analogous conditions are found in apparently normal joints as a result of trauma or infection. 5. The after-treatment must be intelligently carried out, especially with reference to osteoporosis or atrophic bone changes that can be avoided by intensive physiotherapy.

Odelberg,[63] from Waldenström's clinic, reflects an entirely different point of view from the generally accepted one in regard to arthroplasty in old tuberculous ankylosis. He reports seven successful results, five in the elbow, and two in the hip. Two of these cases were ankyloses resulting from operative excision for tuberculosis. Discussing this further, he says that when Waldenström obtains wound healing by primary intention following a radical excision for tuberculosis with complete removal of the capsule, preferably in one piece and with conscientious eradication of all bone foci, he considers this in principle an indication for arthroplasty from six to twelve months afterward, during which time, however, the patient must be kept under observation.

Campbell[64] reports the end-results in sixteen cases of arthroplasty of the knee joint, which, added to his previous series of twenty-four cases, makes a total of forty operative cases. He says that the report on his first group of cases was not encouraging, but from his later experience, especially in the last year, he believes that arthroplasty of the knee is justifiable in well selected cases and gives an excellent chance of obtaining satisfactory motion. He reserves the operation for cases of ankylosis that have been caused either by traumatism or by an acute infectious arthritis due to such organisms as staphylococcus, streptococcus, pneumococcus or gonococcus. In his group of sixteen cases, twelve patients had solid bony ankylosis of the patella, femur and tibia, two fusion of the patella and femur, and two fibrous ankylosis. Ten cases obtained motion of from 30 to 90 degrees, two were failures, and in two cases with ankylosis of from seven to eight years' duration there is slight instability, which should improve with muscle training.

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63. Odelberg, A.: Acta chir. Scandinav. **57**:331 (Aug. 14) 1924.
64. Campbell, W. C.: Ann. Surg. **80**:88 (July) 1924.

[ED. NOTE.—The two articles by Campbell on arthroplasty are thorough and painstaking. The basis on which he selects his cases is reasonable, and in large measure explains his excellent results. When followed out, however, it is readily seen that from a large number of cases only a few could be selected for a mobilizing operation. We believe that this is the measure of the inadequacy of modern arthroplastic technic, but until more perfect methods of operation are devised, the surest guarantee of success will remain careful selection of cases. End-results of mobilizing operations can only be judged at the end of five or ten years, as there is a definite tendency after apparently brilliant postoperative results for joints to lose their motion in time, or for their motion to become painful. In this sense, Campbell's cases should not be considered as end-results, although the immediate results seem definitely encouraging. In respect to the views of Odelberg and Waldenström concerning arthroplasty in old tuberculous joints, we can only believe their experience is small, as is suggested by the small number of cases reported, or that their knowledge of the pathology of joint tuberculosis is limited. Many of the bone foci of tuberculosis are so small as only to be visible on microscopic examination, and any approximation of complete removal of the infected tissue is impossible. Such foci may remain latent for years, only to light up under the influence of fresh trauma or of motion. To attempt arthroplasty in such cases is to court disaster.]

Bifurcation Operation of Lorenz.—Haas,[65] describing the technic of Lorenz' bifurcation operation for congenital dislocation of the hip, states that it is of the utmost importance to place the proximal end of the shaft of the femur in the acetabulum and to obtain solid union of the fragments. The femur must be sectioned at a point directly opposite the center of the acetabulum. Originally he employed a transverse osteotomy, but now he cuts the femur in oblique frontal direction from below, posteriorly, to above, anteriorly, thus obtaining a much larger surface of contact and preventing flexion of the upper fragment. Since he has used this method he has always obtained bony union. The leg is fixed in about 45 to 60 degrees abduction, about as much as can be compensated for by tilting of the pelvis and slight hyperextension. The capsule is used at the most ideal material for interposition, and thus a new joint is formed allowing a very useful degree of motion in flexion, although abduction is somewhat limited. In unilateral cases the result is apparent lengthening, due to the abducted position; in bilateral cases there is a certain shortening, which is, however, without practical importance. In bilateral cases it is safer to operate on the two hips at different times, but it is perfectly possible to do both in one sitting. Thus far sixty patients have been operated on in Lorenz' clinic, and the results have

65. Haas, J.: Ztschr. f. orthop. Chir. **43**:481, 1924.

been excellent. The patients walk with solid support, Trendelenberg's sign becomes negative, and the marked lordosis disappears. The endurance is increased, and there is absence of pain. Haas believes that in view of the favorable results the attempt to reduce the femoral head in old cases by open operation should be given up. The method is also stated to be of value in cases of pseudarthrosis of the neck of the femur due to fracture and in cases of congenital coxa vara.

Osteochondromatosis of the Hip.—Sutherland [66] reports the case of a boy of thirteen years, with osteochondromatosis of the hip joint. There had been a history of several falls, but four weeks before examination, while he was riding a bicycle, there had been sudden locking of the hip. Roentgen-ray examination showed multiple osteocartilaginous bodies within the hip joint. At operation a lobulated osteocartilaginous growth was removed from the bone along the line of the reflection of the synovial membrane from the anterior trochanteric line. About thirty loose bodies were removed from the joint itself, and several could not be reached because of their deep position.

[ED. NOTE.—In view of the fact that the loose bodies that are left in the joint are sure to cause trouble, we believe that it would have been better to dislocate the head and make certain of their removal.]

Lesions of Ulnar Nerve in Region of Elbow.—Platt [67] points out that nerve lesions associated with recent fractures of the lower end of the humerus are rare. Late involvement of the ulnar nerve, occurring as long as fifty years after fracture of the humerus in childhood, does occur. Recurring dislocation of the ulnar nerve may also cause a neuritis. For all these conditions, Platt believes operation to displace the nerve to the front of the elbow is the most logical and effective procedure.

Fascial Transplants.—Gallie and LeMesurier [68] give their experience with the transplantation of fibrous tissue in various conditions, such as injuries to tendons and ligaments, paralytic deformities, facial paralysis, ptosis of the viscera, hernia, and in certain ununited fractures. Success has been uniform in ruptures of the small tendons of the fingers and in divisions of the larger patellar and Achilles tendons. Its use in habitual dislocation and in fracture of the patella is described, also the operations in hernia, visceroptosis, shoulder paralysis, and ptosis of the eyelid. They conclude that in the repair of certain anatomic defects, the transplantation of fascia, aponeurosis and tendon is a valuable surgical procedure, and that transplants of these tissues, when given an adequate supply of lymph, continue to live practically unchanged. They heal to

66. Sutherland, C. G.: Radiology **3**:285 (Oct.) 1924.
67. Platt, H.: Brit. M. J., Oct. 11, 1924, p. 659.
68. Gallie, W. E., and LeMesurier, A. B.: Brit. J. Surg. **12**:289 (Oct.) 1924.

tissues with which they are placed in contact by ordinary scar. The employment of these tissues as transplants in the form of sutures removes the element of chance that attends healing by scar tissue.

The same authors,[69] in a second article, report the use of free transplants of fascia in the form of living sutures in approximately 100 cases of hernia of all varieties. Up to the present there have been no recurrences.

[ED. NOTE.—We are familiar with this work of Gallie and LeMesurier and regard it as a model of what a complete piece of work should be. Careful experimental and histologic study preceded the clinical application. A precise technic is necessary in fixing the transplants, and this is based on principles previously established. Gradually the field of usefulness of the method has broadened, until now it appears almost limitless. The work represents a very definite contribution to surgical progress.]

Mobilization of Stiff Metacarpophalangeal Joints.—Heyman [70] has obtained encouraging results in certain cases of stiff metacarpophalangeal joints that have resisted all forms of conservative treatment and physical measures, by operation with transverse section of the posterior portion of the joint capsule, followed by temporary fixation of the fingers in extreme flexion. The modification of the banjo splint is useful after the position of flexion has been obtained and is preferable because of its comparative inconspicuousness, simplicity, and usefulness in obtaining passive motion in conjunction with traction.

Reconstructive Surgery of the Hand.—Bunnell,[71] in a painstaking article, discusses reconstructive surgery of the hand. He emphasizes the following main principles: Preliminary to operation the wrist and fingers must first be put in functioning positions. The joints must be mobilized before the tendons are repaired, or no motion will result. The use of a tourniquet, preferably a blood pressure band, is essential. This may be used for one hour in safety, but two hours is too long and is followed by a generalized tissue reaction. Local anesthesia, especially with epinephrin, is to be avoided as it lowers the resistance of the tissue. A second operation should not follow until after the lapse of several months; otherwise, scar tissue which delays the recovery of function results. The final result is not to be expected until after the completion of the softening up process; this often takes a year. In respect to after-treatment, more faith is to be placed in active exercise and use than in physiotherapy. Most important of all is the time factor.

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69. Gallie, W. E., and LeMesurier, A. B.: Use of Free Transplants of Fascia as Living Sutures in the Treatment of Hernia, Arch. Surg. **9**:516 (Part 1) (Nov.) 1924.

70. Heyman, C. H.: Surg., Gynec. & Obst. **39**:506 (Oct.) 1924.

71. Bunnell, Sterling: Surg., Gynec. & Obst. **39**:259 (Sept.) 1924.

Special splints are often required, and the surgeon must be familiar with them. Very careful records should be kept showing the exact condition before and after operation. The article does not lend itself to abstract, and the original is deserving of study.

Osteotomy of the Os Calcis.—Nicolaysen [72] reports two cases treated by Gleich-Brenner's osteotomy of the os calcis. The first was a case of flatfoot. An incision was made from the internal malleolus across the Achilles tendon to the external malleolus. The heel cord was lengthened and a curved osteotomy performed through the os calcis, the posterior fragment being displaced downward toward the plantar surface. A good result was reported one year after operation. The second case was one of pes cavus. The same operation was performed, with the exception of the lengthening of the heel cord, but this time the os calcis was displaced upward. The result was excellent at the end of six months.

[ED. NOTE.—We believe that this procedure may have a definite place in the correction of certain cases of severe pes cavus or in old fractures of the os calcis with flattening, but we believe its use as a means of correcting flatfoot is both illogical and unwise.]

FRACTURES

Fracture of the Ribs by Muscular Violence.—Palfrey [73] reports a series of ten cases of fracture of the ribs, either complete or incomplete, in which the trauma was provided by muscular action due to a peculiarly violent cough from a prevalent tracheitis. The ribs most commonly involved were the seventh and eighth in the midaxillary line. They were treated by adhesive strapping and all the patients recovered.

Fractures of the Upper End of the Humerus.—Santee,[74] analyzing seventy-five cases of fracture of the upper end of the humerus, states that the majority of them occur in persons beyond midlife, and that the resulting disability is usually marked and prolonged. He believes that the disability is due chiefly to the associated injury of the soft tissues about the site of fracture. The position of wide abduction and external rotation is the one of choice for fixation. In a number of cases, this position must be attained gradually. While recognizing the value of various types of ambulatory splints, the writer feels that the conditions encountered are best and most comfortably met by recumbent traction and overhead suspension. Massage and physiotherapy are aids in treatment, but the best and quickest results reward the cooperative and

72. Nicolaysen, K.: Norsk. Mag. f. Lægevidensk. **85**:664 (Aug.) 1924.
73. Palfrey, F. W.: Boston M. & S. J. **191**:498 (Sept. 11) 1924.
74. Santee, H. E.: Ann. Surg. **80**:103 (July) 1924.

intelligently active patient. For this reason, women who resume their household duties early are apt to regain function and strength more rapidly than men.

Fracture of the Carpal Scaphoid.—Troell [75] believes that fracture of the carpal scaphoid is produced by a forced radial abduction of the wrist with simultaneous dorsal flexion, whereas simple dorsal flexion leads to Colles' fracture. The deciding factor is the palmar flexion of the scaphoid when the hand is forced into radial abduction and dorsal flexion. Troell is unable to find any evidence to support the theory of congenital partition of the scaphoid. In his studies he has examined hundreds of fetal wrists of various ages and has found no single case of bipartite scaphoid.

Fibrous Ankylosis of the Wrist and Fingers.—Gill [76] calls attention to the fact that fibrous ankylosis of the fingers, due to prolonged swelling, is one of the most easily acquired disabilities of the hand, and that the treatment is most discouraging. It may result from any fracture or dislocation in the upper extremity where long fixation is necessary or from extensive wounds or infection of the hand or forearm. Especially in Colles' fracture and other conditions must early attempts at prevention be made. Early movement of the fingers and wrist is essential to ensure good function. Often extremely useless hands may follow Colles' fracture after admirable reduction and fixation, while good, useful hands may result when the deformity has not been reduced, but the joints of the hand have been in use while union was taking place. The hand should not be allowed to hang down, and massage with all motions that can be allowed should be begun early.

[ED. NOTE.—Gill's observations on stiff hands are not new, but they are of the kind that cannot be stressed too often. In this day there is no excuse for delay in beginning motion in Colles' fracture. The fingers should be free from the start, and movement of the wrist and radio-ulnar joints should be begun within seven days.]

Fracture of the Neck of the Femur.—Schmorl [77] has made a careful study of thirty-four specimens of fracture of the neck of the femur. He finds that senile osteoporosis does not necessarily depend on arteriosclerosis, as he has seen it in the absence of that condition. It is usually most evident in the situations where the fractures most commonly occur. He has also found not infrequently various other abnormalities present in the bone, such as cartilaginous foci, exostoses, angiomas and necrotic foci. The fracture line usually follows a characteristic course,

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75. Troell, Abraham: Acta chir. Scandinav. **55**:490, 1923.

76. Gill, A. B.: Fibrous Anklylosis of Hand Due to Prolonged Swelling, J. A. M. A. **83**:1137 (Oct. 11) 1924.

77. Schmorl: München. med. Wchnschr. **71**:1381 (Oct. 3) 1924.

with steps or teeth. The injury causes a disruption of the spongiosa, which may result in a gap of from 1 to 2 cm. when the fragments are torn apart. Infolding of the capsule may be one of the causes of nonunion, as it was present to a certain degree in 75 per cent. of the cases. Fragments of the torn spongiosa may enter the acetabulum and be the cause of inflammatory reaction leading to the formation of a pannus and complete destruction of the articular cartilage with ankylosis. Complete laceration of the synovial covering of the neck may lead to a complete necrosis of the head in adults, but in younger persons the vessels of the round ligament may suffice for the nutrition of the head. Partial necrosis of the head may follow partial laceration of the synovia. He concludes that active use favors the formation of bone in the scar tissue.

Lindgren,[78] from a study of ninety-five cases of fracture of the neck of the femur, reaches the following conclusions in regard to treatment: Fractures of the neck of the femur should, as a rule, be treated, those of the medial type without exception, in a hospital under proper supervision and repeated roentgen-ray control. All recent cases, when the patients are not decrepit or in poor condition from illness, should be treated by active, nonoperative methods; the medial fractures by reduction and plaster fixation according to the Whitman method; the lateral fractures by reduction and fixation by means of a spica or by extension (adhesive plaster or ice tongs). The deformity should be corrected in every case except when impaction with none or only a functionally inconsequential misapposition is present. In the medial type of fracture, an ideal apposition of the fragments must be obtained and the shortening should be reduced to less than 1 cm. Fixation should be continued for at least twelve weeks and for another month the patient should be kept in bed, during which time mobilization of the hip by active voluntary movement is being accomplished. Weight-bearing should not be permitted before the end of six months. Operation is indicated only in cases of pseudarthrosis with pain or great functional disturbance. In loose pseudarthrosis young patients should be operated on as early as possible; in pseudarthrosis elderly patients should not as a rule be operated on until the end of the first year. He considers the operation of choice in the ununited cases to be the autoplastic bone graft. When this is contraindicated for one reason or another, he recommends the bifurcation operation of Lorenz.

[ED. NOTE.—It is extremely interesting and at the same time gratifying to have this clear announcement of therapeutic principles from Scandinavia, interesting because the reviews are so much in accord with those of American surgeons, and gratifying because it shows that the

78. Lindgren, U.: Acta chir. Scandinav. **57**:55 (July 12) 1924.

fight for a policy of active treatment which has been led by Whitman has borne its fruits in a foreign country. We believe that the Continental surgeons, generally, have not been quick to accept this plan.]

Fractures of the Shaft of the Femur.—Abbott,[79] writing on fractures of the femur with special reference to the treatment of ununited and malunited cases, demonstrates the great therapeutic possibilities of efficient traction and countertraction in conjunction with the Thomas splint and caliper extension after the method of Pearson. By a report of seven cases, he shows that in fractures with malunion, even those of several months' duration, it is possible to cause refracture by manipulation and to obtain union with full length and accurate alinement by caliper traction on a Thomas splint. Manipulation and skeletal extension can be used to correct deformity and to promote union in cases of delayed union and to gain length before operative treatment. He urges that protection with weight-bearing, as provided by a Thomas walking caliper splint, should be accepted as standard in the after-treatment of all fractures of the femur.

David [80] reports an interesting study of the late results in seventy-five cases of fracture of the shaft of the femur in children under the age of 12. He finds that compensatory overgrowth of a shortened femur after fracture may be expected in a growing child. He urges that this should be a consideration of importance in further limiting operative intervention in fresh cases. Another finding of importance as regards treatment is that alinement of the fractured ends to prevent angulation and extension to prevent overriding are of greater importance than end-to-end apposition of the fragments. Not that end-to-end position is undesirable, but union takes place without it provided marked overriding is prevented. The late roentgenologic study of fractures that healed without end-to-end apposition shows a restitution of the shaft practically to normal.

Fractures of Leg and Ankle.—Cochrane [81] reports excellent results in fractures of the leg and ankle from the use of a sectional plaster-of-Paris casing similar to that used by Fiske for correcting congenital clubfoot. He considers it important to have a method of securing retention which will guarantee that when reduction is secured it will not be lost by any alteration of the surgeon's hands during the application of the plaster cast. Separate plaster casings are closely applied over stockinette and cotton padding above and below the seat of injury. These having hardened, the parts can be brought into close apposition and united by a third plaster. Further correction of position if neces-

79. Abbott, L. C.: Fractures of Femur, Arch. Surg. **9**:413 (Sept.) 1924.

80. David, V. C.: Shortening and Compensatory Overgrowth Following Fractures of Femur in Children, Arch. Surg. **9**:438 (Sept.) 1924.

81. Cochrane, W. A.: Brit. J. Surg. **12**:213 (Oct.) 1924.

sary can be obtained by cutting the cast on one side and introducing a wedge to pry the two portions apart. He believes that this represents the method of choice in all cases with displacement in which immediate reduction and fixation are indicated.

Royle [82] reports the use of a sectional plaster casing similar to that described by Cochrane. He employs the method in fractures of the long bones generally and has found it extremely satisfactory.

[Ed. Note.—Some of us have also employed this method in certain fractures and we should like to add our endorsement to that of Cochrane and Royle of its effectiveness.]

Direct Leverage in Reduction of Certain Fractures.—Thomson [83] advocates the use of direct leverage by means of an ordinary dental probe in forearm cases, and by means of steel rods in thigh cases, for securing reduction in obstinate fractures. A small stab wound is made in the skin over the site of fracture, and through this the instrument is thrust until the fragment is engaged. The reduction is performed under the fluoroscope and is brought about by manipulation aided by the direct leverage of the instruments. The reduction is maintained by means of plaster-of-Paris, and the levers are left in the wounds for a period of from seven to eight days, their external ends being embedded in the plaster to help keep the bones in position.

[Ed. Note.—We report this method only for the purpose of condemning it. The blind introduction of metallic instruments and their subsequent manipulation involves trauma to the soft parts and risk of damage to important structures, which is unjustified by any conceivable advantage.]

Operative Treatment of Recent and Ununited Fractures.—Trout [84] reports the results of an investigation of the effects of internal fixation on the healing of fractures. Fractures were produced in rabbits, and it was found that with simple fractures, bony union was obtained in 74 per cent.; with compound fractures, but without internal fixation, bony union was obtained in 70 per cent.; with compound fractures and internal fixation by means of steel plates, bony union was obtained in only 30 per cent. He then made a clinical study of thirty-two patients with regard to the same features. He concludes that the conversion of a simple fracture into a compound fracture is warranted only in exceptional cases, and that the employment of a nonabsorbable internal splint is a factor in the production of nonunion. Metal appliances should always be removed even in the presence of firm bony union, for they

82. Royle, N. D.: M. J. Australia **1**:133 (Aug. 9) 1924.

83. Thomson, J. E. M.: Surg., Gynec. & Obst. **39**:356 (Sept.) 1924.

84. Trout, H. H.: Operative Treatment of Recent Fractures and Nonunion, Arch. Surg. **9**:275 (Sept.) 1924.

frequently give rise to later trouble in the form of osteomyelitis and occasionally to constitutional symptoms which disappear after the removal of the foreign body.

Results of Bone Grafts.—Kirk [85] reports the end-results in a series of 148 consecutive autogenous bone grafts for nonunion of the long bones, performed at the Walter Reed Hospital. Most of the cases were old and baffling, and many of them had been operated on previously with failure. In the first group of noninfected fractures, there were twenty-nine grafts, of which twenty-seven were successful. In the second group there were 129 grafts, of which fifty-three were failures. The majority of these cases were war wounds in which there had been severe damage to the soft parts and chronic osteomyelitis. The loss of bone substance to be bridged by the graft varied from 1 to 5 inches (2.5 to 12.7 cm.), and in these cases the grafts were made three times as long as the gap so as to be thoroughly in contact with good bone. The inlay graft was used in over 60 per cent. of the cases and the intermedullary in 25 per cent. The latter was almost universally successful. No attempt to insert a graft was made until six months after all signs of infection had disappeared.

[ED. NOTE.—There are few more difficult problems for the surgeon than that of pseudarthrosis following compound, infected fractures, especially if there is in addition a large loss of bony substance. We are very fortunate to have this careful and honest analysis of the results of such a large series of cases.]

RESEARCH

Experimental Study of Ununited Fractures with Especial Reference to the Inorganic Bone Forming Elements in the Blood Serum.—Petersen [86] concludes from his experiments on dogs that the healing of fractures has a definite relation to the concentration of inorganic bone forming elements in the blood serum. If the phosphorus content of the blood serum of a dog is reduced by diet to such a degree that the phosphorus and calcium is less than 30, fractures will not unite. If phosphorus and calcium are then raised to their normal level by diet, the fractured bones will unite.

Mineral Content of the Blood in Osteomalacia.—Blum [87] and his co-workers have studied the mineral content of the blood in osteomalacia and conclude that the alkalis, sodium, calcium and potassium are decreased, while the magnesium and phosphorus remain normal. The

85. Kirk, N. T.: J. Bone & Joint Surg. **6**:780 (Oct.) 1924.

86. Petersen, H. A.: Bull. Johns Hopkins Hosp. **35**:378 (Nov.) 1924.

87. Blum, L.: Delaville and Van Caulaert: Compt. rend. Soc. de biol. **91**: 599 (July 25) 1924.

decrease in alkali is not due to an excess of acids, but to a hypo-alkalosis. A diet rich in minerals was without effect in raising the sodium and calcium content of the blood. The changes in osteomalacia are apparently due to a mineral instability of the plasma.

Clinical Deductions Following a Study of Bone Repair.—Bancroft [88] concludes from gross, microscopic and physicochemical studies that the repair of fractures of the bones proceeds along the following line: After fracture there is hemorrhage which may extend into the muscles, fascia and skin. The blood clot becomes organized by the ingrowth of connective tissue. Calcium phosphate and calcium carbonate are deposited on connective tissue stroma in the perivascular areas. These salts are carried in the blood stream partly by colloids and partly by carbon dioxid. There is a change in the hydrogen ion concentration in the vicinity of the fracture which decreases the acidity and apparently causes the precipitation of calcium salts. These calcium salts apparently come from two sources, from the circulating blood and from the fractured ends of the bones. The latter undergo a demineralization and atrophy. Bancroft believes that numerous attempts at reduction of fracture interfere greatly with the eventual union of broken bone, because such tissue destruction with resultant acid products delays the deposition of calcium salt.

Changes in Articular Surfaces in Tuberculous and in Pyogenic Infections of Joints.—Phemister [89] has shown that the following changes take place in pyogenic and tuberculous joints: 1. In pyogenic arthritis, articular cartilage is killed and destroyed primarily and most extensively at the points of contact and pressure of opposing articular surfaces. 2. In tuberculous arthritis, if the joint presents both free and contacted surfaces, the articular cartilage is killed and destroyed first by the direct attack of granulation tissue along the free surfaces. The cartilage is best protected and often stands longest in the regions of contact and greatest pressure in the joint. 3. In tuberculous arthritis, at the points of pressure and contact, the attack of granulations on the cartilage is usually from beneath, resulting in absorption of bony cortex and detachment and thinning of the cartilage. 4. Proteolytic ferments are present in pyogenic arthritis and assist in the digestion of dead cartilage. They are absent in tuberculous arthritis, and dead cartilage which has been detached or which is located on sequestrums may stand for months or years without being destroyed. 5. Secondary invasion of the bone, resulting in sequestrums bordering on the articular surface is rare in pyogenic arthritis but common as a late occurrence in tuberculous

88. Bancroft, F. W.: N. Y. State J. Med. **24**:827 (Sept.) 1924.
89. Phemister, D. B.: Am. J. Roentgenol. **12**:1 (July) 1924.

arthritis. In tuberculosis, the points of contact and pressure are apt to be the seats of bony invasion, and the invasion is often bilateral, producing the picture of "kissing sequestrums." The roentgenographic picture of both diseases varies considerably, but in general evidences of disappearance of cartilage and cortex first at points of contact and pressure suggest pyogenic arthritis while evidences of their preservation longest in these regions and of disappearance in unopposed regions are indicative of tuberculous arthritis.

Reaction of Bone to Various Metals.—Zierold [90] has experimented on dogs to determine whether metal in itself influences the process of repair when implanted in the tissues. He has used gold, aluminum and stellite, and finds that they are tolerated in bone and tend to become encapsulated with little hindrance to the reparative process. In other words, they represent inert material in the tissues, unaffected by the living cells and body fluids. Elsberg, Duval and Danhorn have observed, however, that aluminum is absorbed when implanted in the tissues. Silver and lead are less tolerated by the bone, are easily corroded, and evoke a slightly greater connective tissue response. Zinc goes into solution readily and causes a slight connective tissue stimulation. It also interferes with bone regeneration and does not become encapsulated by it. Nickel has a distinctly injurious effect on bone repair. It is soluble in the tissue and is not tolerated. Contrary to Grove's observation on magnesium, Zierold finds that it has little action other than as a connective tissue stimulant. It retards rather than accelerates bone production. Copper causes definite stimulation to bone production, is very little absorbed, and has a toxic action on the tissues. Alloying copper and aluminum seems to increase this toxic action. Steel and to a less degree iron definitely inhibit bone regeneration. Steel is poorly tolerated and readily soluble, and seems least suitable of all for use in bone surgery.

The Healing of Rickety Bones in Vitro.—Shipley [91] has observed that an isolated piece of bone from a rachitic rat placed in serum or plasma taken from normal animals, or from those with rickets in the process of healing, will begin to calcify in forty-eight hours. Examined microscopically, the bones show that the calcification of cartilage and bone depends, in part at least, on the exercise of cellular activity as well as on the composition of the tissue and that calcification will be more or less independent of the arrangement of the blood vessels.

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90. Zierold, A. A.: Reaction of Bone to Various Metals, Arch. Surg. **9**:365 (Sept.) 1924.

91. Shipley, F. G.: Bull. Johns Hopkins Hosp. **35**:304 (Sept.) 1924.

MISCELLANEOUS SUBJECTS

Myositis Ossificans Traumatica.—Makins,[92] discussing the subject of myositis ossificans traumatica, states that the name should be restricted to a condition consequent on an injury in which the three following factors are associated: First, an injury to the periosteum or bone of sufficient severity to allow the escape of bone cells into the neighboring muscle sheath. Second, hemorrhage from the bone and surrounding tissues. Third, an injury to the muscle sufficient to open its sheath. Clinical observation has demonstrated the regular presence of these three factors, and their capacity to produce the condition has been proved experimentally by Morley and others. The primary treatment in all cases should be complete rest and avoidance of anything likely to increase the vascularity of the affected part, because of the general tendency of the tumors to undergo spontaneous absorption and to leave no serious trace behind them. The bony masses may decrease rapidly in size, but difficulty is likely to be experienced when the tumor is in the fibrous structures about a joint, as for example, the elbow. Here in the later stage of the process operative treatment may be necessary.

Idiopathic Osteopsathyrosis.—Wagoner [93] reports a carefully studied case of osteopsathyrosis or fragilitas ossium. The patient, a negro, aged 38, had at different times, as a result of slight trauma, sustained approximately forty-five fractures of the long bones. The calcium and phosphorus content of the blood were normal, and the bone contained normal amounts of calcium, phosphorus and magnesium. The basal metabolic rate was increased and there was marked exophthalmos, a palpable thyroid, immature genitalia, a shallow pituitary fossa, mild tachycardia, blue sclerae and impaired hearing. No evidence was found of syphilis or infection. No tendency or familial predisposition to fracture could be discovered. One of the legs was amputated, and microscopic examination of the cross-section of the tibia showed a broken and thinned cortex and distended Haversian canals and evidence both of increased bone resorption and new bone formation.

Hyperneurotization of Paralyzed Muscle.—Serra [94] uses the term hyperneurotization to mean implanting a second nerve into a muscle already supplied by a normal nerve. He hyperneurotized the muscle in seven rabbits and found by careful electrophysiologic experiments that the implanted nerve did not act to carry stimuli to the muscle which would cause more than very slight local contractions, unless the healthy nerve were divided and so caused to degenerate. The explanation seems to be that new motor terminal placques are not formed, but if the

92. Makins, George: Brit. J. Radiol. **29**:323 (Sept.) 1924.
93. Wagoner, G. W.: Ann. Surg. **80**:115 (July) 1924.
94. Serra, Giovanni: Chir. d. org. di movimento **8**:617 (Aug.) 1924.

original nerve supply is destroyed the implanted nerve sends fibrils to the existing placques and then it will act nearly as the normal nerve acts in carrying impulses.

Mycetoma.—Audrain [95] reports a case of mycetoma, or Madura foot, treated by a new method so successfully that the former routine treatment of amputation seems to be unnecessary. This patient, a youth of 18, in excellent physical condition, and with a negative Wassermann reaction, had no less than 136 discharging sinuses and scars on his foot and ankle. During a period of eighteen months, he was given eighteen injections each of neo-arsphenamin and mercurochrome-220 soluble. He was discharged with all sinuses healed, and a month later walked 12 miles without any pain.

Clinical Study of Thumb Muscles.—Desfosses [96] emphasizes the extreme importance of the thumb and reports a clinico-anatomic study of its function. Flexion of the proximal phalanx is produced by the flexor brevis and extension by the extensor brevis. Extension of the distal phalanx is produced by the extensor longus. Abduction of the metacarpal of the thumb is produced by the long abductor pollicis. Abduction of the first phalanx is caused by the short abductor to the thumb. Adduction of the thumb is produced by the adductor which brings the first metacarpal toward the hand and brings forward the second metacarpal. Opposition of the thumb is accomplished by rotation of the metacarpal, which turns the tumb inward toward the palm and opposes it to the other fingers. This movement is the most vital motion of the thumb, and loss of it is sufficient greatly to impair the usefulness of the hand. The short abductor is used to turn the proximal phalanx on its axis so that it may be opposed to the second and third fingers. Opposition to the fifth finger is brought about by the short flexor of the thumb. The movement of opposition is largely dependent on motion of the metacarpal of the thumb, and this it is that governs the chief use of the hand, namely, the ability to hold such different sized objects as a pair of pliers, a pen or a needle.

BOOK REVIEWS

AMPUTATIONS, OPERATIVE TECHNIQUE, FORMATION AND AFTER-TREATMENT OF THE STUMP FROM THE STANDPOINT OF PROSTHESIS. By N. T. Kirk. Washington, D. C.: Interpreter Publishing Company, 1924.

This volume represents the first distinctive American contribution to the new literature on amputations and amputation stumps which has been created by the World War. It is based on the author's large

95. Audrain, L. C.: Case of Mycetoma, J. A. M. A. **83**:1165 (Oct. 11) 1924.
96. Desfosses, P.: Presse méd. **76**:1598 (Sept. 20) 1924.

personal experience with these cases at the Walter Reed General Hospital. It is particularly to be recommended for its detailed description of the operations of secondary amputation and plastic closure. This is a procedure of great value for dealing with short stumps which by reason of insufficient covering are unsuitable for prosthesis; it has not hitherto been adequately described. The volume is nicely gotten out and the illustrations are clear and of value, particularly those showing the standard prosthetic appliances developed by the Surgeon-General's office to meet the war needs.

ARTIFICIAL LIMBS. APPLIANCES FOR THE DISABLED. By Dr. Florent Martin. Geneva: International Labor Office, Studies and Reports, Series E (Disabled Men), No. 5, 1924.

The League of Nations includes medical duties among its manifold functions. This is made evident by a volume just issued, dealing with artificial limbs. The purpose of its publication is to make available for international use all information of help to the disabled. The work has been done by Dr. Martin of Brussels, whose pioneer work with temporary prosthesis and in the construction of artificial limbs on anatomic principles is well known. The book is a catalogue of prosthetic appliances and practically every form of apparatus in use anywhere today is both described and illustrated, usually with mechanical drawings. The amputation problem itself also is considered in all its varied aspects. As a compendium and reference work it has great value. The book may be had in either French or English on application to the International Labor Office at Geneva.

FRACTURES AND DISLOCATIONS, IMMEDIATE MANAGEMENT, AFTER-CARE AND CONVALESCENT TREATMENT, WITH SPECIAL REFERENCE TO THE CONSERVATION AND RESTORATION OF FUNCTION. By Philip D. Wilson, A.B., M.D., F.A.C.S., Instructor in Orthopedic Surgery, Harvard Medical School, and William A. Cochrane, M.B., Ch.B., F. R. C. S., Edinburgh, University Tutor in Clinical Surgery, University of Edinburgh. With 978 Illustrations and a Foreword by Dr. Daniel F. Jones, Chief of Staff, Massachusetts General Hospital Fracture Service, pp. 790. Philadelphia and London: J. B. Lippincott Company.

We, with one exception (Philip D. Wilson), wish especially to commend this recent book on fractures and dislocations and their after-care with reference to function. The plan of this book is new, and it fulfils to an unusual degree the purpose for which it was written. It is based on the wide experience of two surgeons who were very active during the war and have since been intimately concerned with the treatment of fractures, the one on the very active and especially organized Fracture Service of the Massachusetts General Hospital, and the other in the

rich wards of the Royal Infirmary in Edinburgh under Sir Harold Stiles. It does not include many of the old classical methods of treatment of fractures which have been found wanting in our experience, but gives one or two methods of treatment that have been found most practical and simple of application. These methods are illustrated in detail by photographs of the actual patient and apparatus, that the general practitioner may follow them with ease and assurance. The full outline of the essential anatomy of the bones and joints, ligaments, muscles, vessels and nerves which precedes the consideration of the fractures of the different regions of the body is one of the most valuable portions of the book. It is all important that the surgeon should be familiar with the normal anatomy before he attempts to diagnose the individual lesion. The general practitioner has sorely needed such a work, since he often is obliged to meet these emergencies. No class of injuries has received less satisfactory immediate treatment and rational after-care as regards function than fractures and dislocations. We commend the book highly both in purpose and accomplishment.

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